Postprandial Hypotension in Older People

Thesis submitted by

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Dedication

I dedicate this thesis to my parents, without whom

I would not be where I am today,

and to my dear husband, Remesh,

whose unwavering support has helped me grow,

day by day.

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Publications and Awards Arising from Thesis

Published articles

Nair, S., Visvanathan, R. & Gentilcore, D. (2015). 'Intermittent walking: A potential treatment for older people with postprandial hypotension', *Journal of the American Medical Directors Association*, 1–5.

Nair, S., Piscitelli, D., Tam, K., Nair, P.S. & Visvanathan, R. (2014). 'Neck of femur fractures within two hours of a meal', *Journal of Geriatrics and Gerontology Research,* 3:5.

Published abstracts

Nair, S., Gentilcore D., Visvanathan R. (2012). 'The effects of a postprandial blood pressure decline following a glucose drink on gait parameters in healthy older volunteers', *Australasian Journal on Ageing*, volume 31, issue supplement s1, p 2.

Awards

RM Gibson Prize for the best platform presentation by an advanced trainee in geriatric medicine at the 2013 Australia and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting in Adelaide, South Australia (Appendix 4).

Best oral presentation in the Clinical Research Group at the Basil Hetzel Institute and The Queen Elizabeth Research Day 2013 (Appendix 4).

Best oral presentation in the Clinical Research Group, at the Basil Hetzel Institute and The Queen Elizabeth Research Day 2014 (Appendix 4).

Conference presentations

'The effects of a postprandial blood pressure decline following a glucose drink on gait parameters in healthy older volunteers'. Oral presentation at the Australia and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting in Sydney, 2012.

'Intermittent walking: A potential treatment strategy for older people with postprandial hypotension'. Oral presentation at the Australia and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting in Adelaide, South Australia, 2013.

'Is postprandial hypotension a possible contributor to hip fractures in older people' at the Basil Hetzel Institute and The Queen Elizabeth Research Day, 2013.

'The postprandial blood pressure decline following a glucose drink affects gait detrimentally in older people' at the Basil Hetzel Institute and The Queen Elizabeth Research Day, 2014.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Abstract

Postprandial hypotension refers to an excessive decline in blood pressure that occurs following a meal. This occurs commonly among older people and is clinically relevant as it is associated with multiple negative consequences, including falls, which itself has significant detrimental medical, psychological, functional and socio-economic consequences. As the ageing population is increasing, postprandial hypotension is going to be an increasingly prevalent condition. Where possible, it is important to prevent this, in order to maintain an older persons' functional independence. Therefore appropriate management strategies are required to address postprandial hypotension. However, current management strategies are sub-optimal. Non-pharmacological strategies have not been specifically evaluated in older people and available options may not be widely applicable, whereas pharmacological strategies may result in potential adverse effects

(a) The primary goal of the research reported in this thesis was to determine the effects of low-intensity, intermittent walking on postprandial blood pressure among older people with PPH. The hypothesis was that low-intensity, repeated exercise would attenuate the hypotensive effects of a glucose drink in older people with PPH, and that this effect would be sustained for the duration of the exercise. The results of the investigation provided evidence for the first time that intermittent walking exercise is an effective and practical therapeutic option for older people with PPH.

(b) There is a gap in our knowledge about the ways in which gait parameters can be influenced by a decline in blood pressure after a meal, as observed in people with PPH. We therefore initiated a study designed to determine whether a postprandial decline in SBP following a 50 g glucose drink would affect gait parameters in older people with and without PPH. We hypothesised that the decline in blood pressure among older people with PPH would detrimentally affect gait parameters compared to the effect on older people without PPH. The results showed that postprandial BP decline does affect gait parameters, an insight which will assist in understanding the relationship between PPH, gait impairments and falls.

(c) In addition, we sought to determine in older hospitalised patients the prevalence of NOF fractures occurring within two hours of a meal and the factors associated with these fractures, since this is the time when postprandial hypotension occurs. Results indicated that one-fifth of fractures occurred within two hours of a meal. Patients who sustained a NOF fracture within two hours of a meal were more likely to be from residential care, experience symptoms associated with hypotension before a fall and have a history of recurrent falls in the preceding 12 months than patients who fell after more than two hours following a meal.

Postprandial Hypotension in Older People

Chapter 1

Introduction

World population is experiencing unprecedented ageing. While in the past 60 years, there has only been a modest increase in the proportion of people aged 60 years and above, from 8% to 10% of the total population (Beard et al., 2011), in the next 40 years, this proportion is expected to rise to 22%, which translates into a dramatic increase from 800 million to two billion people over the age of 60 during the first half of this century (Beard et al., 2011). This increase will be most apparent among the 'older old', those individuals aged 80 years and above, whose population will increase by a factor of 26; whereas the population of individuals aged between 60 and 80 years will increase by a factor of ten (Christensen et al., 2009; Beard et al., 2011).

Globally, life expectancy has steadily increased from 48 years in the 1950s to 68 years in 2005 and is expected to increase to 75 years by 2050 (Beard et al., 2011). Australia, similar to other developed nations, has an expanding ageing population. In Australia, the percentage of people aged 75 years and above is expected to increase from 6.4% of the population in 2012 to 14.4% in 2060, which is an increase of four million people (ABS, 2008). Although the ageing trend began in the developed world, developing nations are experiencing accelerated ageing, and 62% of all people aged 65 years and above now live in developing countries (Kinsella & He, 2009). Therefore, unlike developed countries, developing nations will need to cope with getting old before they get rich (Lunenfeld & Stratton, 2013).

This demographic shift is a positive reflection of advances in medicine and socioeconomic development, together with a declining fertility rate. The initial increase in global ageing was a result of a decline in infant and maternal mortality, which led to a larger cohort of people reaching older age. Subsequent reductions in mortality have been a consequence of improved socio-economic standards combined with medical advancements (Beard et al., 2011).

1.1 Healthy ageing

As the ability to live longer increases, there is an increasing percentage of functional disabilities (Christensen et al., 2009). The prevalence of disability, increases from 15% among younger adults to 45% among adults aged 45 - 74 years to 82% among individuals aged 85 years and over (ABS 2008). Therefore, there is a need to emphasise active ageing by adding quality life to years rather than years to life without quality. This view is held by major organisations, such as the World Health Organization, which dedicated its annual World Health Day in 2012 to ageing, and the European Union which designated 2012 as the Year of Active Ageing and Solidarity between Generations (World Health Organization, 2007). Active ageing is defined as 'the process of optimising opportunities for health, participation and security to enhance quality of life as people age' (World Health Organization, p. 12, 2002).

An important component of successful active ageing is compression of morbidity to ensure that the number of years spent living healthily is optimised, which will translate into improved productivity and a longevity dividend (Beard et al., 2011). A key element of active ageing is preventive health policy. The World Health Organization active ageing framework acknowledges the importance of preventing health decline in older people, which includes limiting disability and falls (World Health Organization, 2007). Falls in older people have been specifically identified as an important public health issue and a major contributor to disability as falls are associated with numerous adverse physical, psychological and economic effects (Tinetti et al., 1988; Kannus et al., 1999; Rubenstein & Josephson, 2002; Moller, 2003).

1.2 Falls in older people

A fall is defined as an event which results in a person coming to rest inadvertently on the ground, floor or other lower level (Close et al., 1999). Falls are common, with a prevalence of 30% among community dwelling older people and 50% among older people living in residential care facilities (Tinetti & Speechley, 1989; Kannus et al., 2005; Rubenstein, 2006; Tinetti & Kumar, 2010).

1.2.1 Consequences of falls

Falls are associated with significant detrimental physical and psychological morbidity (Kannus et al., 2005; Magaziner et al., 1990). Two-thirds of accidental deaths among people aged 65 years and above are due to falls (Deandrea et al., 2010).

Injuries and disability. Fall-related injuries account for more than 80% of injury related hospital admissions in individuals over 65 years of age (Kannus et al., 1999; Lord et al., 2001; Weir & Culmer, 2004). Furthermore:

- Falls account for 10% to 15% of visits to the emergency department (Runge, 1993).

- Among older people who fall, 50% are unable to rise without assistance, which may result in dehydration, pressure ulcers, or rhabdomyolysis (Tinetti et al., 1993).

- A third of falls result in injury requiring medical attention or restriction of activities for at least one day (CDC, 2008).

- Major injuries, such as fracture occur in 5% to 10% of falls among community-dwelling older people and increases to 10% to 30% of falls among older people in residential care (Sattin et al., 1990; Rubenstein & Josephson, 2002).

- A third of these fractures comprise hip fractures, which has a particularly dismal outcome with a mortality of 33% in the first year (Hannan et al., 2001).

- Hip fractures also result in permanent functional disabilities in 32% to 80% of older people when they occur (Magaziner et al., 1990; Jette et al., 1987).

Psychological. The negative psychological implications of falls in older people are significant. Fear of falling, as defined by Tinetti and Powell (1993, p. 35), is 'a lasting concern about falling that leads to an individual avoiding activities that he/she remains capable of performing'. This is common behaviour among 27% to 50% of older people, with a higher prevalence reported among individuals with a history of falls (Tinetti & Powell, 1993; Reelick et al., 2009). The resulting loss of confidence and self-restricted activity then spirals down into a cycle of functional decline, depression, feelings of helplessness, and social isolation (Rubenstein & Josephson, 2002). Falls in the older person are associated with institutionalisation as 50% of older people hospitalised for fall-related injuries are discharged to residential care facilities (Sattin et al., 1990).

Economic. From an economic perspective, the consequences of falls on the health care system are significant. Between 1994 to 1995, fall-related injuries in Australians aged over 65 years were estimated to cost AUD$406.4 million (Mathers & Penm, 1999). If indirect and non-medical costs are included, the cost escalates to more than AUD$1,000 million (Moller, 1998). With the ageing of the Australian population, the projected cost of health care for fall-related injuries is expected to triple to AUD$1375 million by 2051, including the need for an additional 2500 hospital beds per year (Moller, 2003).

1.2.2 Falls prevention

Given that there has been a worldwide increase in the total number of fractures secondary to falls over the past 50 years which is projected to continue (Kannus, 2006), falls are going to pose a future challenge which it is vital to address. Among older people who fall and injure themselves, half have a history of falling more than once (Tinetti & Kumar, 2010). This provides an opportunity for secondary prevention strategies. The importance of falls prevention has been highlighted in a retrospective analysis of causes of serious falls which determined that two-thirds of deaths due to falls were possibly avoidable (Rubenstein, 2006). Falling is considered to be one of the most significant preventable health problems facing older people (Duxbury, 2000).

A key component of falls prevention strategies requires the identification of risk factors associated with falls. The risk factors for falls in older people are typically multifactorial and the falls risk increases from 8% among those with no risk factors to 78% among those with four or more risk factors (Tinetti et al., 1988) (Table 1.1). Falls are a consequence of the interaction of extrinsic and intrinsic risk factors (Tan & Kenny, 2006; Stevens, 2005; Tromp et al., 2001). It is therefore essential to identify all falls risk factors, because modifying these factors in a multidisciplinary approach has been shown to reduce falls by 64% (Close et al., 1999). Postprandial hypotension (PPH) and gait impairment are examples of two intrinsic risk factors relevant to falls prevention (Tan & Kenny, 2006; Tinetti et al., 1988; Rubenstein, 2006) and will be discussed in greater detail in Chapters 2 and 3.

Table 1.1   Risk factors for falls in older people

Risk factors	
Intrinsic	Musculoskeletal Muscle weakness Joint stiffness
	Gait impairment
	Balance disorders
	Cardiovascular Low blood pressure due to postural hypotension, postprandial hypotension Arrhythmia Aortic stenosis
	Cognitive impairment or depression
	Medications
	Sensory loss
	Acute medical illness
	Previous history of falls
Extrinsic	Environmental
	Footwear

1.3   Research aims

The research reported in this thesis focused primarily on blood pressure changes following a meal and is presented in the form of three studies in Chapters 4, 5 and 6. The aims and hypotheses of these studies were:

1. To determine the effects of low-intensity, intermittent walking on the systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) responses to a 50 g glucose drink in older people with PPH. *The **hypothesis** was that low-intensity, repeated exercise would attenuate the hypotensive effects of a glucose drink in older people with PPH and that this effect would be sustained for the duration of the exercise.*

2. To determine if a postprandial decline in SBP following a 50 g glucose drink affects gait speed, variability in stride length, double support time and swing time in older people with and without PPH. *The **hypothesis** was that the decline in blood pressure among older people with PPH would detrimentally affect these gait parameters when compared with older people without PPH.*

3. To determine in older hospitalised patients the prevalence of NOF fractures occurring within two hours of a meal and the factors associated with these fractures.

1.4   The organisation of the thesis

The chapters of the thesis are ordered as follows:

Chapter 2 is a review of PPH including the definition, pathophysiology, symptoms, consequences and management of this condition.

Chapter 3 provides an overview of gait changes in older people, including the definition of gait, gait analysis, prevalence and consequences of gait impairments, in particular falls.

Chapter 4 discusses a study evaluating the effect of postprandial blood pressure decline on gait parameters among subjects with and without PPH.

Chapter 5 presents a study investigating the role of intermittent low-intensity exercise on PPH. This chapter has been recently published in the peer-reviewed *Journal of American Medical Directors Association* (JAMDA). The published article has been included in this thesis as Appendix 1.

Chapter 6 reports findings from a study undertaken to determine the prevalence of NOF fractures occurring within two hours of a meal and the factors associated with these fractures. This chapter has been recently published in the peer-reviewed Journal of Gerontology and Geriatrics Research. The published article has been included in this thesis as Appendix 2.

Chapter 7 summarises the research findings of this Masters thesis and presents possible future research directions.

Postprandial hypotension

Summary

Postprandial hypotension (PPH), which results in a reduction in SBP, is increasingly recognised as an important clinical entity. PPH is common, its prevalence varying according to the cohort of older people being considered. Concurrent co-morbidities and the clinical setting – older people in the community, residential care or within hospitals - for example, may influence prevalence. The pathophysiology of PPH is multifactorial and remains unclear. Even if asymptomatic, it is associated with numerous adverse effects, including falls. Hence, identifying and addressing PPH is important in preventing adverse consequences. Treatment of PPH may be divided into non-pharmacological and pharmacological strategies. Within the former group, exercise has been proposed as a potential treatment strategy for PPH, but has been explored in only a few studies.

This chapter provides the foundation for understanding meal-related blood pressure reduction. As the research reported in this thesis was focused on PPH among older people, only studies involving people above the age of 65 years are discussed. There is particular emphasis on studies highlighting the relationship between PPH and falls, and the role of low-intensity exercise in managing PPH. Research gaps were identified during the course of the research, leading to the research aims outlined in Chapters 4 and 5.

2.1 Defining PPH and measuring for prevalence

2.1.1 Definition of PPH

PPH was first reported in 1977 in a 65 year old gentleman who developed symptoms associated with a significant decline in SBP following an oral glucose drink (Seyer-Hansen, 1977). PPH is defined as a 20mmHg reduction in SBP within two hours of the commencement of a meal (Jansen & Lipsitz, 1995) or when SBP decreases to less than 90mmHg provided that the pre-ingestion SBP is greater than 100mmHg (Mathias et al., 1989; Jansen & Lipsitz, 1995). This is the definition used to diagnose PPH in Chapters 4 and 5. The fall in BP can occur at any time from 15 minutes to 75 minutes after meal ingestion, although a nadir typically occurs with between 30 to 60 minutes of meal consumption (Aronow & Ahn, 1994), before returning to baseline by 180 minutes after meal ingestion (Berry et al., 2003). PPH is said to be most prevalent after breakfast (Puisieux et al., 2000; Vloet et al., 2003).

2.1.2 Prevalence of PPH

PPH is common among older people, although the reported prevalence differs as a result of heterogeneity in study methodology and the differing health characteristics of the subjects researched (O'Mara & Lyons, 2002; Trahair et al., 2014). The methodology can be variable in terms of the meal composition and timing, the posture of the subject, the technique used to measure BP, the duration of postprandial BP monitoring and the use of concurrent medications (Jansen & Lipsitz, 1995; Trahair et al., 2014).

The prevalence of PPH has been researched among older people living in the community, residential care, hospitals and among older people with different co-morbidities, such as hypertension, diabetes mellitus, Parkinson's, and autonomic dysfunction; and the reported prevalence varies with the presence of illness.

Older people living in the community, residential care and hospitals. PPH occurs even among healthy community dwelling older people with prevalence rates ranging from 7% to 40%, (Van Orshoven et al., 2010; Peitzman & Berger, 1989; Lipsitz & Fullerton, 1986). The wide variation in the prevalence rates is possibly due to differences in study methodology. For example, with a highly sensitive method of measuring the BP using beat-to-beat finger BP monitoring in a small study of 20 subjects, the highest prevalence of 40% was reported (Van Orshoven et al., 2010). In addition, postprandial BP was monitored for 135 minutes following a meal.

Other studies have relied on conventional methods to measure BP and monitored the BP for a shorter duration of 60 minutes (Peitzman & Berger, 1989; Lipsitz & Fullerton, 1986), and reported lower prevalence. As the fall in BP to achieve the diagnosis of PPH can occur as late as 75 minutes following a meal, the shorter studies may be under-reporting the prevalence. Furthermore, the majority of prevalence studies conducted among older people in the community were small, involving less than 100 subjects.

The prevalence of PPH within residential facilities (Table 2.1) ranged from 24% to 38% (Aronow & Ahn, 1994; Vaitkevicius et al., 1991; Le Couteur et al., 2003; Son & Lee, 2012), and includes the only prevalence study conducted involving Asians (Son & Lee, 2012). The highest PPH prevalence of 38% was documented in a study which measured postprandial BP only once at 60 minutes following a non-standardised breakfast (Le Couteur et al., 2003). Clinically, this is relevant as it indicates that the diagnosis of PPH can be undertaken in a relatively convenient manner, which is easy to replicate within residential facilities as well as hospitals. Another point to note is that among older people in residential care, even within groups that appeared more frail, such as in the study by Vaitkevicius et al. in which only 16% of subjects were ambulatory (Vaitkevicius et al., 1991) and in the study by Aronow et al., where a third of the subjects were wheelchair bound, (Aronow & Ahn, 1994) the prevalence of PPH did not appear to be markedly higher than the prevalence of PPH among older people in the community. However, as postprandial BP was measured following lunch rather than breakfast, this may have reduced the reported prevalence rates as PPH is most common after breakfast (Puisieux et al., 2000; Vloet et al., 2003).

Table 2.1   Studies investigating prevalence of postprandial BP decline among older people in the community, residential care and hospitals

Study	Setting	Subject characteristics	Methodology	Summary
Van Orshoven et al., 2010	Community	N = 20 Mean age 82 ± 4 years	Meal: subjects' normal breakfast BP assessment: Portapres beat-to-beat finger BP monitoring for 135 minutes	40% had PPH
Smith et al., 2003	Community	N = 5888 Mean age 73 years	Meal: subjects' normal meals BP assessment: mercury sphygmomanometer; at the time of the BP measurement, time of the last meal was noted	SBP measured within one to two hours after a meal was on average 3.8 mmHg lower than SBP at the time of the meal
Peitzman & Berger, 1989	Community	N = 16 Mean age 82 years	Meal: standardised breakfast (mixed meal, 1848 kJ, 30% carbohydrate, 20% protein, 50% fat) BP assessment: equipment not stated; measured every 15 minutes for 60 minutes	25% had PPH
Lipsitz & Fullerton, 1986	Community	N = 21 Mean age 73 ± 6 years	Meal: normal lunch BP assessment: mercury sphygmomanometer; measured every 15 minutes for 60 minutes	7% were found to have a significant decline in postprandial SBP
Son & Lee, 2012	Residential care	N = 121 Mean age 82 ± 7 years	Meal: subjects' normal lunch BP assessment: mercury sphygmomanometer measured every 15 minutes for 90 minutes	32% had PPH
Le Couteur et al., 2003	Residential care	N = 179 Mean age 83 ± 7 years	Meal: subjects' normal breakfast BP assessment: ambulatory blood pressure monitoring once at 60 minutes	38% had PPH
Aronow & Ahn, 1994	Residential care	N = 499 Mean age 80 ± 9 years 32% wheelchair bound	Meal: subjects' normal lunch BP assessment: mercury sphygmomanometer measured every 15 minutes for 75 minutes then at 120 minutes	25% had PPH
Vaitkevicius et al., 1991	Residential care	N = 113 Mean age 78 ± 9 years 16% of subjects ambulatory	Meal: standardised lunch (mixed meal, 650 kcal, 65% carbohydrate, 15% protein, 20% fat) BP assessment: automated sphygmomanometer every 15 minutes for 90 minutes	36% had PPH
Van Orshoven et al., 2010	Geriatric inpatients	N = 22 Mean age 84 ± 5 years	Meal: Subjects' normal breakfast BP assessment: Portapres beat-to-beat finger BP monitored for 135 minutes	91% had PPH

Study	Setting	Subject characteristics	Methodology	Summary
Lubart et al., 2006	Older, orally and tube-fed hospitalised patients	N = 50 with percutaneous endoscopic gastrostomy; mean age 81 ± 9 years N = 50 with naso-gastric tube; mean age 74 ± 12 years N = 50 orally fed; mean age 78 ± 8 years	Meal: Standardised lunch (mixed meal, 600 kcal, 65% carbohydrate, 15% protein, 20% fat) BP assessment: automated sphygmomanometer every 15 minutes for 90 minutes	43% of the total patients had PPH No significant difference in PPH prevalence between groups
Vloet et al., 2005	Hospital	N = 80 Mean age 80 ± 7 years	Meal: standardised liquid breakfast meal (mixed meal, 100 ml liquid glucose and 100 ml milk containing 65 g carbohydrate, 4 g protein 2g fat) BP assessment: ambulatory blood pressure monitoring every 10 minutes for 90 minutes	67% had PPH
Lagro et al., 2012	Falls clinic	N = 313 Mean age 78 ± 8 years	Retrospective cohort Meal: standardised liquid (292 kcal drink containing 100 ml glucose and 100 ml lactose-free milk; 65 g carbohydrate, 4 g protein, 2 g fat) BP assessment: Finapress beat-to-beat finger BP monitoring for 75 minutes Medications: withheld overnight	58% subjects had PPH

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Among hospitalised older people, in three small studies involving less than 100 subjects, the prevalence of PPH was clearly higher, ranging from 43% to 91% (Van Orshoven et al., 2010; Lubart et al., 2006; Vloet et al., 2005). This included a study by Lubart et al., which compared postprandial BP changes among older people on percutaneous endoscopic gastrostomy and nasogastric feeding with older people on oral feeding, and demonstrated that the prevalence of PPH was similar in these three groups (Lubart et al., 2006). A very high PPH prevalence of 91% was reported by Van Orshoven et al., which is likely attributable to the highly sensitive method of measuring BP using beat-to-beat finger BP monitoring (Van Orshoven et al., 2010). In the only study conducted in a falls clinic, approximately half of older people who presented to a falls clinic had PPH (Lagro et al., 2012).

To date, there have been no studies investigating the prevalence of PPH in patients with fractures and in Chapter 6 we describe exploratory research to determine the prevalence of hip fractures occurring within two hours of a meal.

Patients with hypertension, Parkinson's, autonomic dysfunction and other conditions. The prevalence of PPH among older hypertensive subjects has been investigated in three studies, two of which included more than 200 subjects (Barochiner et al., 2013; Zanasi et al., 2012). Among this group, the prevalence of PPH varied widely from 27% (Barochiner et al., 2013) to 73% (Zanasi et al., 2012) which is possibly due to the increased intensity of BP monitoring and the older cohort of patients in the study by Zanasi et al. These two studies highlight the feasibility of detecting PPH using ambulatory BP undertaken in the subject's home, rather than in a clinic or hospital setting.

Among older people with autonomic dysfunction, PPH is very common, with a prevalence of 100% (Lipsitz et al., 1993; Robertson et al., 1981). PPH also occurs frequently among older people with Parkinson's disease (PD), with prevalence rates ranging from 40% to 100% (Loew et al., 1995; Tsukamoto et al., 2013; Mehagnoul- Schipper et al., 2001; Ejaz et al., 2006), possibly related to the presence of concurrent autonomic neuropathy (Chaudhuri et al., 1997). The use of ambulatory BP undertaken in the subject's home in two of these studies (Tsukamoto et al., 2013; Ejaz et al., 2006) emphasises that this is a useful and sensitive method for diagnosing PPH. PPH prevalence studies, among other co-morbidities as described in Table 2.2, included only 13 subjects or less. Therefore, it is important to undertake larger studies before firm conclusions can be drawn.

Table 2.2   Studies investigating prevalence of postprandial BP decline among older people with co-morbidities

Study	Co-morbidity/Setting	Subject characteristics	Methodology	Summary
Barochiner et al., 2013	Hypertensives	N = 230 Median age 74 years	Meal: Subjects' normal lunch BP assessment: subject assessed home automatic sphygmomanometer 60 minutes before and after lunch	27% had PPH
Zanasi et al., 2012	Hypertensives Cardiology clinic	N = 401 Mean age 78 ± 11 years	Meal: Subjects' normal meals BP assessment: 24 hour ambulatory BP monitoring every 15 minutes	73% had PPH
Jansen et al., 1987	Hypertensives vs controls	N = 10 with hypertension N = 10 controls without hypertension	Meal: Standardised liquid drink (75 g glucose in 300 ml water) BP assessment: equipment not stated	Hypertensives demonstrated a a larger postprandial BP decline (17mmHg) compared to individuals without PPH (6mmHg)
Tsukamoto et al., 2013	Parkinson's disease	N = 37 Median age 75 years	Meal: Subjects' normal meals BP assessment: 24 hour ambulatory BP monitoring every 15 minutes during the day and every 30 minutes at night	71% had PPH
Ejaz et al., 2006	Parkinson's disease	N = 13 Mean age 77 ± 6 years	Meal: Subjects' normal meals BP assessment: 24 hour ambulatory BP monitoring every 15 minutes during the day and every 30 minutes at night	100% had PPH
Mehagnoul- Schipper et al., 2001	Parkinson's disease	N = 17 Mean age 75 ± 2 years	Meal: standardised liquid meal (mixed liquid meal, 292 kcal, 65g carbohydrate, 4 g protein, 2 g fat) BP assessment: Finapress finger beat-to-beat BP monitoring	82% had PPH
Loew et al., 1995	Parkinson's disease	N = 10 Mean age 81 ± 9 years	Meal: standardised lunch (mixed lunch, 2500 kJ, 50% carbohydrate, 10% protein, 35% fat BP assessment: semi-automated sphygmomanometer monitoring every 30 minutes	40% had PPH
Lipsitz et al., 1993	Autonomic neuropathy	N = 10 Mean age 65 ± 16 years	Meal: standardised liquid meal (400 kcal drink containing 40% carbohydrate, 15% protein, 45% fat) BP assessment: automated sphygmomanometer monitoring every BP measured every 5 minutes for 90 minutes	100% had PPH

Study	Co-morbidity/Setting	Subject characteristics	Methodology	Summary
Robertson et al., 1981	Autonomic neuropathy	N = 10 54-74 years old	Meal: standardised meal (456 kcal, 46% carbohydrate, 12% protein, 42% fat) BP assessment: automated sphygmomanometer every 3 minutes for 180 minutes	100% had PPH
Idiaquez et al., 1997	Alzheimer's dementia	N = 10 Mean age 74 ± 6 years	Meal: standardised liquid meal (500 kcal, 54.5% carbohydrate, 14% protein, 31.5% fat) BP assessment: automated sphygmomanometer every 10 min for 120 min	70% had PPH
Zoccali et al., 1989	Renal failure	N = 13	Meal: standardised meal (400 kcal) BP assessment: automated sphygmomanometer	75% had PPH

2.2   Clinical significance of PPH

Symptoms of PPH range from lethargy, giddiness and dizziness to visual disturbance (Jansen & Lipsitz, 1995; Lipsitz & Fullerton, 1986), or to more significant conditions, such as angina (Vaitkevicius et al., 1991) and cerebrovascular accidents (Tabara et al., 2014). Many older people experiencing PPH are asymptomatic (Van Orshoven et al., 2010). However, it has been demonstrated that negative consequences, such as silent lacunar infarcts, occur even among the asymptomatic group (Kohara et al., 1999). Similarly, PPH as an independent predictor of mortality, occurs among asymptomatic subjects (Fisher et al., 2005).

Two other significant consequences of PPH in older people are falls and syncope (Jansen et al.,1995; Puisieux, et al., 2000). Table 2.3 summarises the studies investigating the relationship between falls and PPH. The majority of these studies were conducted in residential care (Aronow & Ahn, 1994; Jansen et al., 1995; Le Couteur et al., 2003). There have been no studies involving community dwelling older people. There were two case control studies, one investigating older people in hospital (Puisieux et al., 2000), which reported that 23% of older patients with falls or syncope experience PPH.

There has only been one longitudinal study, involving 499 subjects, in a residential aged care facility (Aronow & Ahn, 1994). The significance of PPH in predicting future falls was highlighted in this study, in which a greater decrease in postprandial SBP at baseline was found to be an independent risk factor for future falls (Aronow & Ahn, 1997). In a cross-sectional observational study undertaken among 179 older people within a residential facility, a significantly greater postprandial SBP decline was documented among older people who experienced falls than among those who didn't (Le Couteur et al., 2003).

The importance of considering PPH when evaluating hospitalised older people with a history of falls or syncope was emphasised in a study by Puisieux, *et al.* which documented the significantly greater prevalence of PPH among hospitalised older patients with a history of falls or syncope (23%), compared to hospitalised older patients without the same history (9%) (Puisieux, et al., 2000). Among older people in residential care, approximately half who experienced a fall or syncope within two hours of a meal had PPH (Jansen et al., 1995), thus highlighting the relevance of targeting efforts to diagnose PPH among this group.

In the context of the results from these studies, strategies aimed at reducing the postprandial BP decline may potentially reduce the risk of future falls, but to date there have been no intervention trials.

Table 2.3   Studies exploring PPH and falls

Study	Setting	Subject characteristics	Methodology	Summary
Aronow and Ahn 1994 & 1997	Residential care	N = 499 Mean age 80 ± 9 years Frail as 32% wheelchair bound	Longitudinal 29 month study Meal: Subjects' normal lunch BP assessment : Mercury sphygmomanometer, every 15 minutes for 75 minutes then at 120 minutes Medications: not withheld	Mean maximum reduction in postprandial SBP was 21 ± 5 mm Hg in residents with falls in preceding 6 months vs. 13 ± 4 mm Hg in residents without falls (P < 0.001) A marked reduction in postprandial SBP was associated at 29 month follow-up with increased incidence of falls (RR 1.2 CI 1.1-1.2, P < 0.001)
Jansen et al.,1995	Residential care	N = 25 16 subjects with unexplained syncope or falls within 2 hours of a meal; mean age: 83 ± 2 years 9 controls; mean age 80 + 2 years	Case-control Meal: standardised breakfast drink (1680 kJ drink containing 40% carbohydrate, 45% fat, 15% protein) BP assessment: automated sphygmomanometer every 5 minutes for 90 minutes Medications: withheld for 24 hours	50% of older persons with unexplained syncope or falls occurring had PPH with reduction in postprandial mean arterial BP of 17 ± 2mmHg (P < 0.001) vs non-significant decline in SBP of 1± 2 mmHg in the controls
Le Couteur et al.,2003	Residential care	N = 179 Mean age 83 ± 7 years	Cross-sectional Meal: Subjects' normal breakfast BP assessment: ambulatory BP monitoring measured 60 minutes after breakfast Medications: withheld overnight	Postprandial decline in SBP was significantly greater in older people with falls vs. without falls (20 ± 5mmHg vs. 12 ± 4 mm Hg) Post prandial SBP of ≤ 115mmHg was associated with a history of falls (OR 3.7 CI 1.3–11.1, P = 0.013)
Puisieux, et al., 2000	Hospitalised patients in a geriatric ward	N = 156 45 with falls; mean age 81 ± 9 years 75 with syncope; mean age 81 ± 8 years 36 controls; mean age 79 ± 7 years	Case-control Meal: Subjects' normal meals BP assessment: 24-hour ambulatory blood pressure every 15 minutes during day and every 30 minutes at night Medications: not withheld	23% of patients with a falls or syncope experience PPH Number of patients experiencing PPH was significantly higher in the syncope and fall group than in control group (23% vs. 9%, P = 0.03)

2.3 Pathophysiology and treatment of PPH

2.3.1 Pathophysiology

The exact pathophysiology of PPH remains poorly understood, but detailed reviews exist (Trahair et al., 2014; Gentilcore et al., 2006b). The research studies discussed in this thesis have not focused on exploring the mechanism of PPH, however, and we only briefly summarise the pathophysiology of PPH here.

In healthy young and older people following a meal, vasodilatation of splanchnic blood vessels diverts blood to the gastrointestinal tract, resulting in a doubling of blood flow through the superior mesenteric artery and reduced blood return to the heart (Lipsitz, 1983). Hypotension is attenuated by activation of multiple compensatory mechanisms. However, among people with PPH, current evidence points to the interplay between multiple factors, which inhibit compensatory mechanisms, thus resulting in PPH.

Baroreceptor dysfunction may occur among individuals with PPH (Lipsitz, 1983; Jansen et al., 1987), particularly among individuals with hypertension (Lipsitz & Fullerton, 1986; Kawaguchi et al., 2002), which may partly account for the higher PPH prevalence seen in this population group (Barochiner et al., 2013; Zanasi et al., 2012). An impaired gastro-vascular reflex (Fagius et al., 1996; van Orshoven et al., 2004), whereby gastric distension, which usually stimulates sympathetic nerve activity, is blunted (Rossi et al., 1998) also contributes to the manifestation of PPH. The release of vasodilating gastrointestinal hormones (Jansen et al., 1990) and the rate of delivery of nutrients to the small intestine and small intestinal nutrient exposure (Gentilcore et al., 2006a; Jones et al., 2005) are some of the other gut related mechanisms contributing to the development of PPH.

2.3.2 Treatment of PPH

Although there is no definitive treatment for PPH, both pharmacological and non-pharmacological strategies may be beneficial.

Pharmacological therapies. Pharmacological strategies in addressing PPH have been discussed in detail in a recent systematic literature review (Ong et al., 2014), which included 14 studies investigating caffeine, alpha-glucosidase inhibitors, guar gum, octreotide and 3,4-DL-Threo-Dihydroxyphenylserine. These agents have been suggested to attenuate postprandial BP decline

through different mechanisms. Caffeine, an adenosine blocker increases cardiac output, vascular resistance and BP (Onrot et al., 1985; Heseltine et al., 1991; Lipsitz et al., 1994). Acarbose and voglibose, both alpha-glucosidase inhibitors, slow the breakdown of complex carbohydrates, delaying gut glucose absorption (Maruta et al., 2006; Gentilcore et al., 2007). Guar gum delays both gastric emptying and glucose absorption in the small intestine, but its use is limited given its awful taste (Jones et al., 2001).

Octreotide, a somatostatin analogue, inhibits the vasodilation of the splanchnic vasculature by inhibiting vasoactive peptides (Hoeldtke et al., 1986; Jansen et al., 1989). 3,4-DL-Threo-Dihydroxyphenylserine is a norepinephrine precursor that replaces levels of circulating norepinephrine (Freeman et al., 1996). Other pharmacological agents that have been studied in single studies are intravenuos infusion of vasopressin (Hakusui et al., 1991) and the combination of midodrine and denopamine (Hirayama et al., 1993), which have been demonstrated to ameliorate postprandial BP decline among individuals with autonomic neuropathy and PPH, but were not specific to older people.

However, a limitation that has been identified is that only two pharmacological studies have been undertaken in subjects with a formal diagnosis of PPH (Shibao et al., 2007; Lipsitz et al., 1994). In these two studies involving older people with PPH (mean age 65 ± 3 years and 76 ± 9 years respectively), acarbose remained an effective intervention (Shibao et al., 2007) but not caffeine (Lipsitz et al., 1994).

Among older subjects with hypertension, optimising BP control may attenuate postprandial BP decline by reducing baseline BP. This was demonstrated in two studies, whereby the use of nitrendipine or hydrochlorothiazide (Jansen et al., 1988) and isosorbide dinitrate or nicardipine (Connelly et al., 1995) diminished postprandial BP. Among older subjects with stable heart failure, gradual discontinuation of frusemide may be considered as a strategy, as this has been demonstrated to significantly reduced the magnitude of the postprandial fall in SBP in a single study (van Kraaij et al., 1999).

The pharmacological trials described have not focused on older people with PPH specifically or older people who are frail. Therefore, it remains uncertain whether these pharmacological strategies are generalisable to these patient populations. With ageing, physiological changes occur

and there is a greater degree of frailty, a larger number of coexisting conditions, and polypharmacy, where 40% of older people take five to nine medications (Budnitz et al., 2011). All of these factors lead to an increased risk of medication-related adverse events among older people (ElDesoky, 2007; McLean & Le Couteur, 2004). Furthermore, available pharmacological agents to address PPH are associated with adverse effects. For example, 31% of subjects on acarbose experience diarrhoea and most develop flatulence (Chiasson et al., 2003).

Hence, when it comes to treating older people with PPH, non-pharmacological strategies remain the first preference and most practical, avoiding adverse drug events.

Non-pharmacological strategies. Non-pharmacological strategies that can be considered in treating older people with PPH are low intensity exercise, such as walking or dietary modification. Changes in diet include reducing the carbohydrate content of food, replacing glucose and sucrose with fructose or xylose, choosing complex carbohydrates over simple sugars and increasing water consumption immediately before a meal.

However, in the majority of studies exploring non-pharmacological strategies, older people with PPH have not been the primary focus, something we tried to address during the course of the current research.

Exercise

Exercise leads to an extensive list of positive health benefits among older people, extending beyond a potential to attenuate postprandial BP decline. It lowers the risk of cardiovascular disease, type 2 diabetes mellitus, osteoporosis, stroke, breast cancer and colon cancer (Miller et al., 2000), improves psychological function, decreases the incidence of depression in older adults (Singh et al., 2001), and improves physical function (Keysor & Jette, 2001).

During exercise, cardiac output increases to ensure adequate perfusion to the exercising muscles (Halliwill, 2001). This results from increased sympathetic activity and reduced parasympathetic tone, which both lead to increased heart rate and contractility, vasoconstriction of venous vasculature (Halliwill, 2001; MacDonald, 2002), and redistribution of blood from the splanchnic circulation (Puvi-Rajasingham et al., 1997) to the exercising muscles. These mechanisms lead to increased BP during exercise.

However, following the initial increase in BP, there is a subsequent hypotension that may occur anytime from within a few minutes to 60 minutes following exercise, which is termed post-exercise hypotension (MacDonald, 2002). The effects of post-exercise hypotension have been the reason for cautioning against exercise following a meal (Oberman et al., 1999). However, different intensity and forms of exercise affect BP differently. Light exercise does not appear to lead to a decline in SBP, while high intensity exercise is reported to cause an initial increase in SBP followed by a decline (Astrand et al., 1964).

To date, there have only been three studies that have investigated the effect of exercise on post-meal BP in older people (Table 2.4). Two of the three studies were undertaken in a residential aged care setting and involved exercise in the form of a single walk for either 5 or 10 minutes and at 20 or 60 minutes post-meal (Jonsonn et al., 1990; Oberman et al., 1999). The smaller study investigated 14 older subjects with PPH (Oberman et al., 1999). In both studies, exercise attenuated the fall in blood pressure during the walk period, but the effect was not sustained.

The third study (only abstract published) researching exercise and postprandial BP responses differed from the earlier research as it involved healthier older people living in the community who engaged in higher intensity exercise (Gentilcore et al., 2008c). In this study, a single exercise on a stationary bicycle at 70% of the predicted maximum HR over 20 minutes after a glucose drink exacerbated the hypotensive response to a glucose drink, and the effect was sustained until 180 minutes post drink ingestion. Therefore, high intensity exercise should probably be avoided post-meal in older people with PPH. The effects of low intensity exercise on postprandial BP, such as intermittent walks commenced before a meal, remains unknown and is the focus of the research presented in Chapter 5.

Table 2.4 Exercise and PPH

Study	Setting	Subjects	Methodology	Conclusion
Jonsson et al., 1990	Residential care	N = 68 58 older subjects; mean age 87 ± 6 years 10 young controls; mean age 24 ± 3 years Subjects had multiple co-morbidities	Meal: Standardised breakfast (cereal 112 g, one to two slices of toast with margarine, 140 to 196 g of orange juice, 1 cup of decaffeinated coffee) Exercise: Single walk at subjects' usual pace for 5 minutes exercise Monitoring: BP & HR monitored during a standardised series of activities from 0700-1300	SBP returned to baseline among the older (60 minutes post-breakfast) subjects during the exercise Effect sustained only for the duration of the of the exercise
Oberman et al., 1999	Residential care	N = 14 Mean age 88 ± 7 years All subjects had PPH Subjects had multiple co-morbidities	Meal: Subjects' normal breakfast Exercise: Single walk for 10 minutes at subjects' usual pace(20 minutes following standardised breakfast) Monitoring: BP & HR monitored for 60 minutes following breakfast	Exercise transiently ameliorated PPH only for the duration of the exercise BP returned to pre- exercise level 10 min after exercise ceased
Gentilcore et al., 2008c	Community dwelling	N = 10 Age: 67-79 years No subjects had PPH Excluded subjects with co-morbidities, such as hypertension	Meal: Glucose drink (300 ml drink containing 75 g glucose) Exercise: Single high intensity exercise-exercising on a stationary cycle to maintain a HR equivalent to 70% of their predicted maximum for a duration of 20 minutes Monitoring: SBP & HR monitored for 210 minutes following glucose drink	Exercise after a meal accentuated post-meal SBP decline for 120 minutes

Water

Studies investigating the role of water in postprandial BP decline have been summarised in Table 2.5. The ingestion of water causes gastric distension, which stimulates the gastro-vascular reflex, thus modulating the postprandial hypotensive response (Jones et al., 2005). Two studies investigating the hemodynamic effects of drinking water were specifically conducted among subjects with PPH and autonomic failure (Deguchi et al., 2007; Shannon et al., 2002). In both studies, drinking 350 ml water immediately before a meal reduced the magnitude of the postprandial BP decline and in the study by Shannon et al., a larger water volume of 480 ml reduced the decline in BP even further (Shannon et al., 2002). This effect was sustained throughout the 90 minutes following the meal. Therefore, drinking a larger volume of water was more effective in reducing postprandial BP decline among older subjects with PPH.

The BP attenuating effects of water have also been demonstrated among older people without PPH (Gentilcore et al., 2008b; Grobéty et al., 2014; Jones et al., 2005). Water volumes necessary to reduce postprandial BP ranged from 300 ml to 500 ml, whereas consuming only 100 ml was not as effective (Grobéty et al., 2014). In these studies, water was consumed rapidly within three to four minutes before the meal. In view of these results, the volume of the glucose drink used in the current research was limited to 200 ml as larger volumes were shown to mitigate postprandial BP responses as a result of gastric distension (Gentilcore et al., 2008b; Jones et al., 2005).

In summary, one large glass of water (i.e., at least 300 ml) consumed within three minutes immediately before a meal may be a simple therapeutic option to be considered as this attenuates postprandial BP decline.

Table 2.5   Summary of studies investigating water and postprandial BP decline in older people

Study	Subject characteristics	Methodology	Summary
Deguchi et al., 2007	N = 5 Mean age 63 ± 6 years Community dwelling All subjects had PPH and autonomic failure	Unblinded, non - randomised Intervention: 350 ml of water consumed before a standardised breakfast (380 cal, 52 g carbohydrate,15g protein,9g fat) BP monitored every 5 min for 90 min	Postprandial BP declined less (by 13mmHg) with water consumption This effect was sustained throughout the 90 minutes following a meal
Shannon et al., 2002	N = 18 Mean age 70 ± 2 years Community dwelling All subjects had PPH and autonomic failure	Unblinded, randomised study Intervention: 350 ml and 480 ml water consumed before a standardised breakfast (414 cal, 52g carbohydrate, 14g protein, 17g fat) BP monitored every 5 min for 90 min	480 ml of water reduced postprandial BP decline by 21mmHg 350 ml of water reduced postprandial BP decline by 13mmHg This effect was sustained throughout the 90 minutes following a meal
Gentilcore et al., 2008b	N = 8 Age ranging 65 - 76 years Community dwelling Excluded subjects with co-morbidities such as hypertension No subjects had PPH	Single-blind, randomised Intervention on three separate days • 50 g glucose in 300 ml saline intraduadenally • 50 g glucose in 300 ml saline intraduadenally and intragastric infusion of 500 ml water • intraduadenal saline infusion and intragastric infusion of 500 ml water BP monitored every 3 minutes for 120 minutes	Intragastric administration of saline markedly attenuated hypotensive response to intraduodenal glucose for 60 minutes
Grobéty et al., 2014	N = 12 Mean age 67 ± 1 years Community dwelling No subjects had PPH	Crossover study on two study days 500 ml and 100 ml water consumed over four minutes before a standardised breakfast (mixed meal 1708 kJ, 60% carbohydrate, 31% fat, 9% protein) Beat to beat BP monitored for 90 minutes	Greater postprandial decline in SBP following 100 ml vs 500 ml (-6.4 mmHg vs -3.3 mmHg, P < 0.05) Therefore 500 ml water reduced postprandial BP decline significantly more than 100 ml water; this effect was sustained throughout the 90 minutes following meal
Jones et al., 2005	N = 10 Mean age 74 ± 1 year Community dwelling Excluded subjects with co-morbidities such as hypertension No subjects had PPH	Single-blind, randomised Subjects studies on four randomised study days and consumed a study drink of either • 200 ml water containing 25 g glucose • 200 ml water containing 75 g glucose • 600 ml water containing 25 g glucose • 600 ml water containing 75 g glucose Drink ingested within 3 minutes BP monitored every 3 minutes for the first 60 minutes, and then every 15 minutes intervals for a further 120 minutes (total 180 minutes)	Within 3 minutes of consuming the 600 ml drinks, SBP increased significantly vs no increase with 200 ml Increase in SBP was transient SBP was higher for the 25 g and the 75 g glucose drink in 600 ml (compared to the 200 ml drinks).

Macronutrient composition is known to influence the hypotensive response to a meal (Jansen & Lipsitz, 1995). Among the macronutrients, carbohydrate, particularly glucose, has the greatest effect on BP (Jansen et al., 1990; Heseltine et al., 1991; Visvanathan et al., 2005). Earlier studies seem to suggest that fat and protein have no effect (Potter et al., 1989; Jansen et al., 1990), but other studies, including more recent studies by our group, appear to contradict these findings (Hoeldtke et al., 1985; Bannister et al., 1987; Sidery et al., 1993; Visvanathan et al., 2006; Gentilcore et al., 2008a). The type of carbohydrate also affects the degree of postprandial BP decline; glucose and sucrose cause a postprandial BP reduction, but not fructose (Jansen et al., 1987; Visvanathan et al., 2005) or xylose (Vanis et al., 2011); and simple sugars cause a larger magnitude decline in postprandial SBP compared to complex carbohydrates (Heseltine et al., 1991). Hence, reducing the carbohydrate content of food, and replacing glucose and sucrose with fructose or xylose and choosing complex carbohydrates over simple sugars may be appropriate dietary modifications.

Meal size

There is limited evidence that patients with PPH may benefit from replacing large meals with smaller and more frequent meals, which may be associated with less splanchnic diversion of blood, hence, reducing the magnitude of postprandial BP decline (Puvi-Rajasingham & Mathias, 1996). However, this has only been investigated in one study in younger people with autonomic failure and PPH (Puvi-Rajasingham & Mathias, 1996); and research involving older people, especially those with PPH is necessary before further recommendations can be made for this population group.

Meal temperature

There is evidence that there are specific warm and cold sensitive receptors in the gastrointestinal tract, and a colder meal is associated with a modest slowing of gastric emptying, which then has the potential to reduce postprandial BP decline (Sun et al., 1988). This possibility was further explored among 15 healthy older subjects (mean age 74 ± 3 years) whereby subjects consumed a test drink served either cold (5 °C) or warm (50°C) (Kuipers et al., 1991). The cold drink caused an initial

rise of 4mmHg in mean arterial BP, following which BP remained relatively unchanged, whereas the warm drink caused a reduction of 8mmHg in mean arterial BP. Therefore there is insufficient evidence to recommend consumption of cold drinks or meals.

2.4   Conclusion

To summarise, PPH is common in older people across all care settings and is of clinical relevance due to its association with falls. The prevalence of PPH in older people experiencing injuries from falls, such as fractures, are however yet to be investigated. Chapter 6 describes the research reported in this thesis to pragmatically explore the prevalence of fractures within two hours of a meal. Although non-pharmacological strategies, such as a glass of water before a meal, cold rather than hot meals, and reduced sugar content may help clinicians treat PPH, there remains a need for better quality studies in older people with PPH. It appears that a single walk may attenuate the fall in BP post meal, but it remains to be seen if repeated walks over a period of time attenuate the fall in BP over a longer period of time. This forms the basis for the research discussed in Chapter 5.

Chapter 3

Gait and falls in older people

Summary

As noted previously, falls are common among older people and are associated with significant physical and psychological morbidity and mortality. There are a variety of risks for falls in older people, and it is essential to identify all falls risk factors and intervene where possible. PPH, which was discussed in Chapter 2 and gait impairment, discussed in this chapter, are examples of two risk factors relevant to falls prevention. To date, there has been no research investigating whether post-meal decline in BP affects gait parameters associated with increased falls risk detrimentally. If it does, then this may be one reason why PPH is associated with increased risk of falls.

Gait is an important human function necessary for maintaining independence. It is presumed to be an automatic function; however, it is recognised to be a highly elaborate, coordinated task. Impairment in gait is more common with advancing age. Early detection of gait changes allows for identification of older people at increased risk of falling. Technological advancements have led to the development of specialised gait analysis devices and we are able to now assess for multiple gait parameters. Not all gait parameters are equally associated with increased falls risk. In this chapter, we discuss how gait is measured and also we identify the gait parameters associated with increased risk of falls.

3.1 Human gait

3.1.1 Physiological control of gait

Gait is presumed to be an instinctive function learnt during childhood and occurring automatically in adulthood. However, considering that gait involves the interplay of motor, sensory, visual, vestibular, cerebellar, cognitive, psychological and musculoskeletal systems, in reality gait is a complex motor task (Lord & Rochester, 2007; Nutt et al., 1993; Sudarsky, 2001).

Physiological changes that occur as people age necessitate more diligence when performing the activity of walking (Beauchet & Berrut, 2006). The interaction between age related physiological changes in gait with co-morbidities results in increased gait impairments (Alexander, 1996; Elble, 1997). Increasing age per se may result in an increase in stride length, cadence and double support time (Callisaya et al., 2008) although some studies dispute that ageing, per se, causes these changes (Kerrigan et al., 1998).

3.1.2 Gait parameters

Walking consists of a series of repetitive events termed the gait cycle (Maki, 1997). A complete gait cycle is the period between the first contact of two consecutive footfalls of the same foot (Hamill & Knutzen, 2003). Gait parameters may be divided into spatial parameters, which are related to distances and temporal parameters, which are related to time (Maki, 1997). The definition of each variable is listed below (Maki, 1997; Hausdorff, 2005; Hollman et al., 2011).

- *Step length (centimetres (cm)*: The anterior-posterior distance from the heel of one footprint to the heel of the opposite footprint.

- *Stride length (cm)*: The anterior-posterior distance between the heels of two consecutive footprints of the same foot; two steps comprise one stride.

- *Stride width/base of support (cm)*: The lateral distance from the heel center of one footprint to the line of progression formed by two consecutive footprints of the opposite foot.

- *Cadence (steps/minute):*The number of steps per minute, also referred to as step rate.

- *Step time (seconds (sec):*The time elapsed from initial contact of one foot to initial contact of the opposite foot.

- *Stride time (sec):* The time elapsed between the initial contact of two consecutive footfalls of the same foot.

- *Stance time (sec):* The time elapsed between the initial contact and the last contact of a single footfall.

- *Swing time (sec):* The time elapsed between the last contact of the current footfall to the initial contact of the next footfall of the same foot.

- *Single-support time (sec):* The time elapsed between the last contact of the opposite footfall to the initial contact of the next footfall of the same foot i.e. when only one foot is in contact with the ground.

- *Double-support time (sec):* The time that both feet are on the ground simultaneously.

- *Gait speed (cm/sec):* Calculated by dividing the distance traveled by the ambulation time.

- *Stride speed (cm/sec):* Calculated by dividing stride length by the stride time.

- *Gait variability:* Gait variability refers to the intra-individual stride-to-stride fluctuations in gait characteristics and is represented by the coefficient of variation (CoV). CoV is calculated by dividing the standard deviation by the mean (of the relevant gait parameter) and multiplying this by 100 (standard deviation)/mean x100. Gait variability is related to the regularity or stability of gait whereby the more irregular the gait, the higher the variability (Hausdorff et al., 2001).

3.2 Gait impairment and the consequences

Gait impairment is common in older people. In a study of 488 older people aged 70 - 99 years living in the community, the prevalence of gait impairment was 35% (Verghese et al., 2006) and in a cross-sectional national survey, 54% of older people aged 85 years and above reported gait impairment (Ostchega et al., 2000).

There is an established association between gait impairment and falls in the literature among older people in the community (Tinetti et al., 1988; Montero-Odasso et al., 2005) and in residential care (Rubenstein & Josephson, 2002; Deandrea et al., 2010). Gait impairment is identified as the second largest contributory cause for falls (Rubenstein & Josephson, 2002; Deandrea et al., 2010) and is associated with a threefold increased risk of falling (Rubenstein & Josephson, 2002). Therefore, it is not surprising that among older people presenting to a falls clinic, gait impairment was present in 85% (Montero-Odasso et al., 2005).

Apart from falls, gait impairment is associated with other adverse consequences, such as reduced mobility (Verghese et al., 2006; Brach et al., 2007), dementia (Verghese et al., 2002), institutionalisation (Verghese et al., 2006) and increased mortality (Bloem et al., 2000; Verghese et al., 2006). Hence, gait may be viewed as a surrogate marker for health and function in the older

person. It has been suggested that the presence of gait impairment may reflect the existence of early, preclinical disease (Snidjers et al., 2007), creating an opportunity for preventive strategies to be implemented to halt the progression to clinical disease.

3.2.1 Assessing gait

Early gait changes are too discrete to be detected by the naked eye and, unfortunately, the first symptom of a gait impairment may be an injurious fall (Sattin, 1992). Therein lies the role of gait analysis, which provides a more accurate and objective manner through which gait impairment can be identified and changes to gait parameters can be monitored.

Gait analysis has evolved over time with advances in technology. In the pre-computer era (Baker, 2007), simple visual observation (Eastlack et al., 1991; Krebs et al., 1985), stop-watches (Wall & Scarbrough 1997; Youdas et al., 2000) and paper walkways (Clarkson 1983; Heitmann et al., 1989) were used. This progressed in the post-computer era to the use of footswitches, which are sensors embedded in shoes (Maki 1997; Barrett et al., 2008), to sophisticated technology devices such as the GAITRite®, which is a portable electronic walkway (Bilney et al., 2003) (Figure 3.1).

Figure 3.1   **Participant walking on the GAITRite®**

The GAITRite®, which was used in the study discussed in Chapter 5, is a portable electronic walkway embedded with pressure sensors that are activated as the subject walks the length of the mat (Bilney et al., 2003). The walkway is connected through an interface cable to a computer installed with the GAITRite® software, which processes and stores the spatial and temporal parameters (Bilney et al., 2003). The advantage of GAITRite® is that subjects walk over the walkway without the hindrance of wires or markers, unlike other gait analysis equipment (Bridenbaugh & Kressig, 2011).

In addition, data can be rapidly and easily obtained for each step in the entire gait trial (Menz et al., 2004). The use of GAITRite® has enabled gait analysis to be undertaken not only in gait laboratories, but more widely in clinical settings (Kressig & Beauchet, 2006) without requiring attachment of monitoring devices, such as footswitches or extensive training (Verghese et al., 2009).

Studies have been performed to evaluate the validity of GAITRite® against previous gait analysis tools with favourable results (McDonough et al., 2001, Selby-Silverstein & Besser, 1999, Cutlip et al., 2000, Bilney et al., 2003, Youdas et al., 2000). The GAITRite® has shown strong concurrent validity and test-retest reliability in older people, in addition to being a portable and reliable tool for the objective assessment of gait (Bilney et al., 2003, Menz et al., 2004, van Uden & Besser, 2004, Wittwer et al., 2008, McDonough et al., 2001).

Test–retest reliability is high, with reliability coefficients that exceed 0.85 for measures including velocity, stride length and double support time (McDonough et al., 2001, Bilney et al., 2003). Furthermore, the validity of the GAITRite® measurements of stride length is not affected by walking speed (Bilney et al., 2003). Older people who require the use of a walking aid to ambulate can also be included in gait analysis by manual editing of the computer data (Verghese et al., 2009), which enables the inclusion of a wider spectrum of older people. The GAITRite® is able to assess the following gait parameters: gait speed, cadence, stride length, stride width, stride time, stance time, swing time, single support time, double support time, and gait variability.

3.2.2   Gait parameters associated with falls

Among the various gait variables able to be assessed by the GAITRite®, not all have been shown to be associated with falls, fracture or fear of falling in older people. Gait speed, stride length variability, and double-support time and swing time variability, appear to be the most clinically relevant in terms of association with falls in older people (Dargent et al., 1996; Chu et al., 2005; Biderman et al., 2002; Montero-Odasso et al., 2005; Quach et al., 2011; Liang et al., 2014; Besser et al., 2001; Verghese et al., 2009; Callisaya et al., 2011) (refer Table 3.1).

Table 3.1   Gait variables associated with falls

Study	Gait parameter	Subject characteristics	Methodology	Summary
Dargent-Molina et al. 1996	Gait speed	N = 7575 Mean age 80 ± 4 years Community dwelling women	Prospective cohort over 1.9 years Gait analysis: 6-meter walk	Gait speed was an independent predictor of fall-related femoral neck fracture
Chu et al., 2005	Gait speed	N = 1517 Mean age 73 ± 6 years Community dwelling	Prospective cohort over 12 months Gait analysis: 5 metre walk test	Gait speed was an independent predictor of falls
Biderman et al., 2002	Gait speed	N = 283 Mean age 71 years Community dwelling	Prospective cohort over 12 months Gait analysis: 5 metre walk test	Gait speed <0.5 m/s was an independent predictor of falls
Quach et al., 2011,	Gait speed	N = 763 Mean age 78 ± 5 years Community dwelling	Prospective cohort over 18 months Gait speed analysis: 6-meter walk	U-shaped relationship between gait speed and falls • Subjects with gait speed >1.3 m/s, and < 0.6 m/s, are at a higher risk than those with normal gait speeds (1.0–1.3m/s) • Gait speed decline > 0.15 m/s per year predicted greater risk of falls
iang et al., 2014	Gait speed	N = 230 Mean age 85 ± 4 years Community dwelling older men	Prospective cohort over 12 months Gait speed analysis: 6-meter walk	Gait speed < 0.5 m/s was an independent risk factor for falls
Montero-Odasso et al., 2005	Gait speed	N = 102 79 ± 4 years Community dwelling	Prospective cohort over 2 years follow-up Gait analysis: 10m walk	Gait speed was an independent predictor of falls
Verghese et al., 2009	Multiple gait parameters: gait speed, cadence, stride length, swing time, double support time, stride length variability, swing time variability	N = 597 Mean age 80 ± 5 years Community dwelling Included older people who required to walk with walking aids	Prospective cohort over 20 months Gait analysed with GAITRite®	The strongest predictors of falls and the only predictors of injurious falls was increased stride length and swing time variability • 10 cm/s decrease in gait speed was associated with an increased risk for falls

Study	Gait parameter	Subject characteristics	Methodology	Summary
Callisaya et al., 2011	Multiple gait parameters : gait speed, step length, step time, cadence, double support time, step width, variability in step length, step time, double support time and step width	N = 412 Mean age among fallers, non-fallers and multiple fallers 71 ± 7 years, 72 ± 6 years, 74 ± 8 years Community dwelling Able to walk without walking aids	Prospective cohort over 12 months Gait analysed using GAITRite®	Gait parameters associated with increased risk of multiple falls in a linear manner • Variability in step (stride) length and double support time Gait parameters associated with increased risk of multiple falls in a non-linear manner • Gait speed, cadence and step time variability
Maki, 1997	Multiple gait parameters: gait speed, stride length, double-support time, stride width, variability in speed, stride length, speed & double-support	N = 85 Mean age 82 ± 6 years Community dwelling Able to walk without walking aids	Prospective cohort over12 months Gait analysed with footswitches	Gait parameters independently associated with falls but little evidence of an association with fear • Increased variability in stride length, speed and double-support time Gait parameters associated with fear but little evidence of an association with falls • Reduced speed, reduced stride length, increased double-support time Gait parameters associated with both falls and fear • Increased stride width
Taylor et al.,2012	Multiple gait parameters : gait speed, stride length, cadence, double support time, variability in step (stride) length and stride time	N = 64 Mean age 81 ± 7 years Community dwelling All had cognitive impairment	Prospective cohort over 12 months Gait analysed using GAITRite®	Gait parameters associated with multiple fallers (≥2 falls in 12 months) • Reduced gait speed and stride length, increased double support time • Increased step (stride) length variability
Besser et al., 2001	Multiple gait parameters: variability in gait speed, double support time, single support time, step time, step length, stride length, and stride width.	N = 74 Age range 67 - 96 years Community dwelling	Prospective cohort over 5 months Gait analysed with GAITRite®	The most predictive measures for falls were variability in • Stride length • Double support times • Single • Stride velocity
Chamberlin et al., 2005	Multiple gait parameters: gait speed, stride length, step width and double support time	N = 95 Mean age 74 ± 8 years Community dwelling Able to walk without walking aids	Cross sectional Gait analysed using GAITRite® Fear of falls assessed	Gait parameters associated with fear of falls • Reduced gait speed and stride length • Increased stride width and double support time
Delbaere et al.,2009	Multiple gait parameters: gait speed, step(stride) length, cadence, double-support time and stride width	N = 44 Mean age 76 ± 5 years Community dwelling	Cross sectional Gait analysed using GAITRite® Fear of falls assessed	Gait parameters associated with fear of falls • Reduced gait speed, stride length and cadence • Increased double support time

Gait speed and falls and fractures. Gait speed is the most extensively investigated gait parameter (Dargent et al., 1996; Chu et al., 2005; Biderman et al., 2002; Montero-Odasso et al., 2005; Quach et al., 2011; Liang et al., 2014), probably due to the ability to measure gait speed easily, quickly and inexpensively without the need for specialised equipment (Bridenbaugh & Kressig, 2011). The majority of these studies have used a timed walk test among healthy, community dwelling older people involving large sample sizes of over 1,000 subjects in two studies (Dargent et al., 1996; Chu et al., 2005) and over 100 subjects in the other studies (Biderman et al., 2002; Montero-Odasso et al., 2005; Quach et al., 2011; Liang et al., 2014).

All studies were conducted over 12 to 24 months. The outcome of the study conducted by Dargent et al. differed in that it specifically highlighted gait speed as an independent predictor of fall related femoral neck fractures (Dargent et al., 1996). In terms of gait speed values or changes in gait speed, a speed of less than 0.5 m/s (Biderman et al., 2002) or a deterioration of gait speed between 0.10 m/s (Verghese et al., 2009) and 0.15 m/s (Quach et al., 2011) has been identified in the literature as a risk factor for future falls. In addition, the study by Quach et al. demonstrated that the relationship between gait speed and falls was U-shaped, as a gait speed of more than 1.3 m/s was also associated with an increased risk of falling (Quach et al., 2011).

Gait variability and falls. Gait variability, particularly stride length and double-support time and swing time variability have been increasingly demonstrated to predict future risk of falls in studies that have used the GAITRite® (Besser et al., 2001; Verghese et al.; 2009, Callisaya et al., 2011; Taylor et al., 2012) or footswitch analysis (Maki 1997). The largest study, conducted by Verghese et al., included nearly 500 subjects and did not exclude older people using a walking aid.

After 20 months, the strongest predictors of falls and the only predictors of injurious falls, were increased variability in both stride length and swing time (Verghese et al., 2009). In two other studies, increased stride length variability was able to predict multiple fallers (Callisaya et al., 2011; Taylor et al., 2012). It is of interest to note that the study by Taylor et al. focused on older people with cognitive impairment, which is an important group to consider as 60% of older people with cognitive impairment fall each year (Laird et al., 2001) and have a higher rate of injurious falls (Muir et al., 2012).

3.2.3 Gait and fear of falling

Fear of falling is prevalent among 27% to 50% of older people, with a higher prevalence reported among individuals with a history of falls (Tinetti & Powell, 1993; Reelick et al., 2009). In gait assessments, it is important to evaluate for fear of falling as it affects gait parameters (Maki 1997, Chamberlin et al., 2005; Delbaere et al., 2009). In two small studies (refer to Table 3.1) involving community dwelling older subjects, the group that demonstrated fear of falling had a significantly slower gait speed, shorter stride length, wider stride width and increased double limb support time (Chamberlin et al., 2005; Delbaere et al., 2009).

In a prospective study by Maki et al., increased variability in stride length, double-support time and gait speed variability were associated independently with falling, and there was little evidence of a relationship between these parameters and the fear of falling, thereby increasing the specificity of the parameters as a falls risk indicator. In contrast, reduced stride length, reduced gait speed and increased double-support time were associated with fear of falling, but showed little evidence of an independent association with falling (Maki, 1997).

3.4 Conclusion

Although we know that both PPH and gait impairment are associated with falls, to date there have been no studies into whether the post-meal decline in BP affects gait. Establishing a relationship between a post-meal decline in BP and altered gait would provide evidence of a possible mechanism through which PPH is associated with falls. To address the research gap, the impact of a post-meal fall in BP on gait was investigated (see Chapter 4). The gait parameters investigated in the research were those that have been demonstrated in the literature to be associated with fear of falling, falls and fractures. These gait parameters are gait speed, variability in stride length, swing time and double-support time.

Chapter 4

The postprandial systolic blood pressure decline following a glucose drink affects gait detrimentally in older people

Summary

PPH and gait impairments are two risk factors for falls in older people. Although the association between falls and PPH has been established, there have been no studies investigating the mechanism by which this occurs. Specifically, information is required to determine whether the falls occur due to PPH having a detrimental effect on gait parameters. The study described in this chapter addresses this issue.

The effect of postprandial SBP decline following the ingestion of a glucose drink was investigated among 24 older subjects. Subjects were studied on three randomly selected days: glucose ('G'), water and walk ('WW') and glucose and walk ('GW') days. Subjects consumed a glucose drink on both the 'G' and 'GW' days, and the 'G' day was used establish which subjects had PPH. Subjects consumed water on the 'WW' day and on both 'WW' and 'GW' days, when gait was analysed.

Thirteen of the 24 subjects demonstrated PPH. Among subjects with PPH, following glucose ingestion there was a significant increase in stride length variability, whilst in subjects without PPH, ingestion of water significantly decreased stride length variability. Since an increase in the variability in stride length has been demonstrated to be a predictor of falls risk in older people, this may be a mechanism by which PPH increases the risk of falls.

4.1   Introduction

Falls are common in older people, with a prevalence of 30% and 50% among community dwelling individuals and older people living in residential care facilities, respectively (Tinetti & Speechley, 1989; Kannus et al., 2005; Rubenstein, 2006). A major consequence of falls is fractures, which pose a considerable public health issue due to the association with detrimental physical and psychological morbidity (Kannus et al., 1999; Rubenstein & Josephson, 2002), as well as significant health care costs (Moller, 2003). Falls risk factors are typically multifactorial (Tinetti et al., 1988) and include PPH and gait impairments (Rubenstein & Josephson, 2002; Jensen et al., 2003).

PPH is a condition that is defined as a 20 mmHg reduction in SBP or a decline in SBP to less than 90 mmHg from a pre-ingestion SBP of greater than 100 mmHg, occurring within two hours of meal commencement (Jansen & Lipsitz 1995; Mathias et al., 1989). As discussed in Chapter 2, there is a strong association between PPH and falls in older people. PPH is present in 25% of older inpatients with a history of falls (Puisieux et al., 2000), 50% of older persons with unexplained falls occurring within two hours of a meal (Jansen & Lipsitz, 1995) and in 58% of older patients seen in a falls outpatient clinic (Lagro et al., 2012).

Gait consists of a series of repetitive events termed the gait cycle (Maki, 1997). As previously discussed (Chapter 3), there is a strong association between gait impairment and falls, such that when the former is evident, the risk of falls is increased (Tinetti et al., 1988; Rubenstein & Josephson, 2002; Montero-Odasso et al., 2005; Deandrea et al., 2010). In a review of 12 studies evaluating falls risk factors among older people, gait impairment was identified as the second largest contributory cause for falls (Rubenstein & Josephson, 2002). Moreover, a recent systematic review and meta-analysis of 74 studies investigating risk factors for falls among community-dwelling older people found that gait impairment ranked as the second strongest falls risk factor (Deandrea et al., 2010). Specific gait parameters that have been robustly associated with falls and are discussed in Chapter 3, include a decrease in gait speed and an increase in the variability of stride length, double-support time and swing time (Dargent-Molina et al., 1996; Verghese et al., 2009; Callisaya et al., 2011).

Previous studies have determined that a relationship exists between (a) falls and PPH (Aronow & Ahn 1994; Jansen & Lipsitz, 1995; Puisieux et al., 2000; Lagro et al., 2012) and (b) falls and gait impairment (Tinetti et al., 1988; Rubenstein & Josephson, 2002; Montero-Odasso et al., 2005; Deandrea et al., 2010); however, it is uncertain if the decline in SBP evident in people with PPH is associated with a change in gait parameters which may then predispose the older person to falls. Hence, the aim of this study was to determine if a postprandial decline in SBP affects gait speed, variability in stride length, double-support time or swing time in individuals with and without PPH.

4.2   Method

4.2.1   Ethics

This protocol was approved by the Human Research Ethics Committees of The Queen Elizabeth Hospital/Lyell McEwin Hospital/Modbury Hospital, Adelaide, Australia (protocol number 2011011). Each subject provided written, informed consent before the commencement of the first study day. All experiments were carried out in accordance with the Declaration of Helsinki.

4.2.2   Subjects

Twenty-four older subjects (16 female, eight male) with and without PPH were recruited either from geriatrician clinics at The Queen Elizabeth Hospital, from lists of research subjects that had previously participated in research studies or via community events related to the Healthy Ageing program undertaken by the Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre. No subject had a history of significant cardiovascular disease (myocardial infarction less than three months earlier, clinical coronary artery disease or symptomatic congestive heart failure), significant respiratory disease, renal impairment, epilepsy, dysphagia, chronic alcohol abuse or excessive cigarette smoking (more than 10 cigarettes a day). Subjects withheld usual medication on the morning of the study days.

4.2.3   Protocol

Each subject was studied on three randomised study days, separated by a minimum of 72 hours. To minimise bias, an online randomisation program (RANDOM.ORG 2014) was used. On each study day, subjects underwent an overnight fast (10 hours for solids and six hours for liquids) and in the preceding 24 hours refrained from alcohol and caffeine containing beverages, and smoking for 12 hours.

The subjects attended the Basil Hetzel Institute at The Queen Elizabeth Hospital at 0830 hours on each day and upon arrival were seated comfortably in a chair. An automated BP cuff was placed around the right arm and following a 10 minute rest period, at t = 0 minutes, subjects ingested a tudy drink. On two of the study days (glucose ('G') and glucose and walk ('GW') days) the drink consisted of a 200 ml drink of 50 g glucose (glucose monohydrate, Fluka Analytical, Sigma-Aldrich Pty Ltd, NSW, Australia) dissolved in water. On the other day, the drink consisted of 200 ml of water alone ('WW' day). The purpose of the 'G' day was to establish which subjects had PPH. Ingestion of a glucose drink is ideal as a mechanism by which to induce a rapid fall in SBP, the magnitude of which fulfils the definition of PPH (Visvanathan et al., 2006). On one day, cardiovascular autonomic nerve function and orthostatic BP were evaluated before the commencement of the study (Visvanathan et al., 2005).

4.2.4 Measurements

Blood pressure. SBP was measured using an automated oscillometric BP monitor (Spacelabs Ultralite 24 hour ABP, JLM Accutek Health Care, NSW, Australia). On all study days, 'baseline' SBP (t = 0 minutes) was calculated as the mean of measurements taken at t = -9, -6, and -3 minutes before ingestion of the drink. SBP was measured every 6 minutes between t = 0 - 60 minutes and then every 15 minutes between t = 60 - 120 minutes.

Gait analysis. Gait parameters were measured using the GAITRite® walkway system (CIR Systems Inc., NJ, USA). This system consisted of a six metre portable walkway with a series of sensor pads activated by mechanical pressure (Menz et al., 2004). Data from the sensors were collected by a series of on-board processors and transferred and stored on a computer. Studies have demonstrated that the GAITRite® measures gait parameters with strong concurrent validity and test-retest reliability in older people (Bilney et al., 2003; Menz et al., 2004; Wittwer et al., 2008; McDonough et al., 2001). Gait speed, variability in stride length, double-support time and swing time were recorded at each subject's self-selected walking speed, i.e. at a pace deemed comfortable by each individual subject.

Gait was analysed on the 'WW' and 'GW' days only. At t = - 20 minutes (i.e. baseline), subjects undertook two practice walks to familiarise themselves with the protocol and GAITRite®, followed by two test walks. Subsequent gait analysis every 30 minutes between t = 30 - 120

minutes involved two test walks only. Gait measurements were calculated as the mean of the two walks (Kressig et al., 2006). To ensure a consistent walking pace, subjects commenced and completed walking approximately two metres before and after the walkway (Macfarlane & Looney, 2008; Kressig et al., 2006), i.e., total walking distance was 10 metres.

Assessment of health status. Subjects were interviewed by a medical doctor using a standardised questionnaire consisting of questions relating to demographic variables, medical history, medication use, history of falls and fear of falls. Global assessment of health status was assessed by calculating the Charlson Comorbidity Index (CCI), a measure of comorbidity which predicts the one-year mortality rate for a patient by taking into account both the number and severity of 19 pre-defined comorbid conditions (Charlson et al., 1997). Each condition is assigned a score of 1, 2, 3 or 6, depending on the mortality risk associated with the condition. The scores are summed and a total score is derived. The one-year mortality rates for the different scores are: '0':12%; '1-2':26%; '3-4':52%; and 'greater than or equal to '5':85% (Charlson et al., 1997).

Fear of falls was assessed using the Falls Efficacy Scale International, a widely accepted tool for assessing concern about falling (Yardley et al., 2005), which has been validated in an Australian population (Delbaere et al., 2010). It is a self-reporting questionnaire, providing information on the level of concern about falls for a range of 16 activities of daily living scored on a four-point scale anchored at one end by 1 = not at all concerned and the other end by 4 = very concerned. A score of 23 and above indicates a high concern about falling (Delbaere et al., 2010).

Cardiovascular autonomic function. Autonomic nerve function was assessed using standardised cardiovascular reflex tests (Ewing & Clarke 1982; Piha 1991). Parasympathetic function was determined by the variation (R-R interval) of heart rate during deep breathing and response to standing (30:15 ratio). Sympathetic function was assessed by the fall in SBP in response to standing. Each of the test results was scored according to age-adjusted predefined criteria as 0 = normal, 1 = borderline and 2 = abnormal for a total maximum score of 6. A score >3 was considered to indicate autonomic dysfunction (Ewing & Clarke, 1982; Piha, 1991). Orthostatic hypotension was determined by measuring SBP in the supine position and then after standing for one and three minutes. Orthostatic hypotension was diagnosed as a decline in SBP of 20 mmHg or more and/or a decline in diastolic BP of 10 mmHg or more between the supine and standing positions (Lipsitz, 1989).

Statistical analysis. Power calculations from preliminary data from the first five subjects enrolled in this study determined that to detect a difference of 10 cm/s in gait speed, 16 subjects with PPH were required to provide an 80% power, at the 0.05 significance level. A value of 10 cm/s was chosen as this has been demonstrated to be clinically relevant (Brach et al., 2010). Gait speed, stride length variability, double-support time variability, swing time variability and SBP were analysed as changes from the baseline. One-way analysis of variance was used to analyse the effects of time on these variables.

The maximum change in SBP, gait speed, stride length variability, double-support time variability and swing time variability were defined as the greatest mean changes from the baseline in each subject at any given time point for each study day, and is reported where a significant change from the baseline is noted. The area under the curve (AUC) between t = 0 - 120 minutes was calculated using the trapezoidal rule and analysed by paired t-test to evaluate a 'treatment' effect for SBP, gait speed, stride length variability, double-support time variability and swing time variability.

Subjects' characteristics were summarised using means and standard deviations, or frequencies and percentages, as appropriate. Comparisons between the characteristics of subject groups were performed using the chi-squared test and independent-samples t-test. All analyses were performed using *SPSS* Version 20 (SPSS Inc., Chicago, IL). Data are presented as means ± standard deviation. A P value < 0.05 was considered statistically significant in all analyses.

4.3   Results

All recruited subjects completed the study, which was well tolerated and no adverse effects were reported. Due to the necessity of completing this Master's thesis, the results of the investigation of the first 24 subjects are presented here. Thirteen of the 24 subjects demonstrated PPH defined by a decline of 20 mmHg in SBP occurring within two hours of consuming the study drink on the 'G' day (Jansen & Lipsitz 1995; Mathias et al., 1989) (Table 4. 1).

Table 4.1 Maximum decline in systolic blood pressure (SBP) among subjects following ingestion of a glucose drink

PPH				NO PPH			
Subject	Baseline SBP (mmHg)	Maximum decline in SBP (mmHg)	Time of maximum decline in SBP* (min)	Subject	Baseline SBP (mmHg)	Maximum decline in SBP (mmHg)	Time of maximum decline in SBP (min)
1	145	25	105	1	127	14	60
2	169	28	30	2	140	11	36
3	145	43	105	3	119	12	90
4	136	23	105	4	126	3	18
5	153	20	18	5	130	11	42
6	134	27	24	6	125	12	18
7	166	23	75	7	150	16	36
8	158	20	105	8	132	14	60
9	144	30	18	9	124	11	30
10	173	47	60	10	151	16	18
11	145	25	120	11	154	3	18
12	132	23	105				
13	133	20	42				
Mean ± SD		27.23 ± 8.86	70 ± 39			11.18 ± 4.58	38 ± 23

Subjects' characteristics are summarised in Table 4.2. When compared with subjects without PPH, those subjects with PPH had a significantly higher ($P = 0.009$) Charlson Comorbidity Index (i.e. indicating that this group had more co-morbidities) and use of antihypertensives ($P = 0.041$). Among subjects with PPH, three had orthostatic hypotension and of these, two had definite autonomic dysfunction. In contrast, among subjects without PPH, only one had orthostatic hypotension and none had autonomic dysfunction. There were no significant differences between the two groups of subjects for all other variables in the assessment of health status.

Table 4.2   Subjects' characteristics

Characteristic	Subjects with PPH (n = 13)	Subjects without PPH (n = 11)	P value
Age, years (mean ± SD)	76.5 ± 4.3	75.9 ± 6.6	0.807
Sex (n/ %) Male Female	4 (33) 9 (69)	4 (36) 7 (64)	0.772
History of falls in preceding 12 months (n/%)	3 (23)	0	0.089
Falls efficacy scale international score (mean ± SD)	18.4 ± 2.2	20.6 ± 7.5	0.334
Orthostatic hypotension present (n/%) SBP / DBP change (mmHg) (mean ± SD)	3 (23) -21.0 ± 9.5 / 6.3 ± 3.5	1 (9) -8 ± 7.6/ 1.3 ± 3.4	0.200
Autonomic dysfunction present (n/%)	2 (15)	0	0.474
Charlson Comorbidity Index (mean ± SD)	2.07 ± 0.9	1.3 ± 0.5	**0.009**
Hypertension (n/%)	7 (54)	2 (18)	0.072
Heart disease (n/%)	2 (15)	0	0.174
Diabetes Mellitus (n/%)	1 (8)	0	0.347
Hypothyroidism (n/%)	2 (15)	1 (9)	0.642
Antihypertensives (n/%)	9 (69)	3 (27)	**0.041**

PPH = postprandial hypotension; SD = standard deviation; n = number of subjects; SBP = systolic blood pressure; DBP = diastolic blood pressure

4.3.1   SBP

Subjects with PPH. There was a significant fall in SBP over time between $t = 0$ - 120 minutes on the 'G' day ($P < 0.005$) but there were no differences on the 'WW' ($P = 0.830$) or 'GW' ($P = 0.520$) days. The mean maximum fall, and time of fall, in SBP on the 'G' day were 27.23 ± 8.86mmHg at 70 ± 67 minutes (Table 4.1). Between $t = 0$ - 120 minutes there was a significant treatment effect for the AUC for the change in SBP from baseline between the study days ($P < 0.005$). During this time, SBP was significantly greater during the 'GW' day than the 'G' day (95% CI = - 1780 – - 389, $P = 0.005$) and there was a trend for a significant increase during the 'WW' day (95% CI = - 1440 - 25, $P = 0.060$) [Figure 4.1 (a1)]. At $t = 120$ minutes, SBP was significantly less than baseline on the 'G' day (136.92 ± 19.22mmHg, $P = 0.005$), but not different from baseline on the 'WW' (151.45 ± 21.61mmHg, $P = 0.137$) or 'GW' (137.92 ± 17.50mmHg, $P = 0.093$) days.

Subjects without PPH. There were no significant differences in SBP over time between t = 0 - 120 minutes on the 'G' (P = 0.172), 'WW' (P = 0.392) or 'GW' (P = 0.685) days. Between t = - 120 minutes there was a significant treatment effect for the AUC for the change in SBP from baseline between the study days (P = 0.021). During this time, SBP was significantly greater during the 'WW' day than the 'G' day (95% CI = 128 - 889, P = 0.014) but not during the 'GW' day (95% CI = - 433 - 303, P = 0.703) [Figure 4.1 (a2)]. At t = 120 minutes, SBP was not different from the baseline on the 'G' (135.00 ± 12.47mmHg, P = 0.843), 'WW' (142.30 ± 12.67mmHg, P = 0.851) or 'GW' (131.89 ± 12.54mmHg, P = 0.372) days.
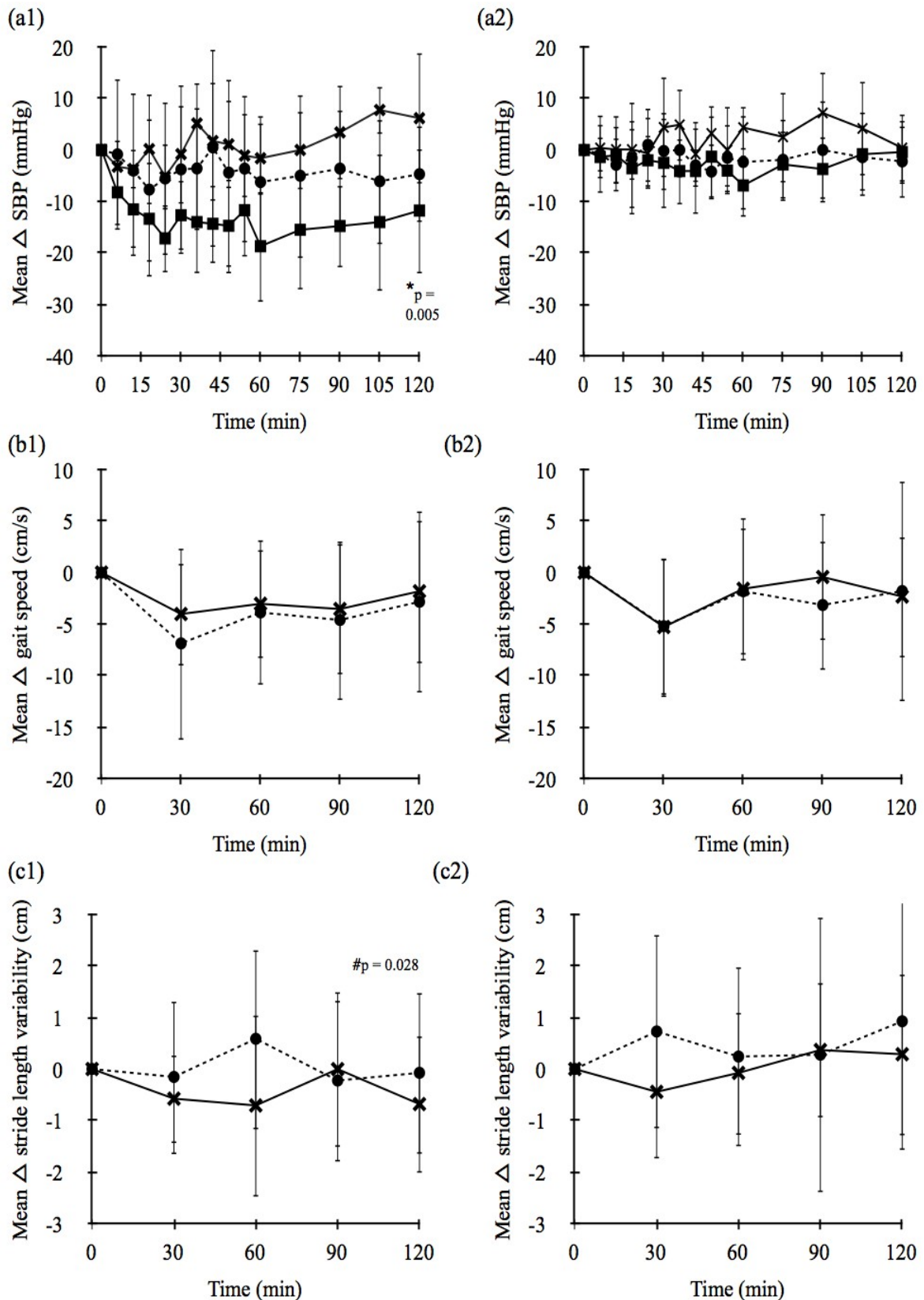
Mean change (Δ) in (a) systolic blood pressure (SBP), (b) gait speed, (c) stride length variability among (1) subjects with PPH and (2) without PPH on the 'G' (■), 'WW' (×) and 'GW' (●) days. Data are mean values with standard deviation represented by vertical bars. *p = 0.005 for the change in SBP from baseline between 'GW' vs 'G'days. # p =0.028 for increase in stride length variability over time between t = 0 - 120 minutes on the 'GW' day.

Figure 4.1   Mean change in systolic blood pressure, gait speed and stride length variability in subjects with and without PPH

4.3.2 Gait speed

Subjects with PPH. There was a trend for a significant decrease (P = 0.054) in gait speed over time between t = 0 - 120 minutes on the 'WW' day but there was no difference on the 'GW' (P = 0.138) day. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in gait speed from the baseline between the 'WW' and 'GW' days (95% CI = - 238 - 469, P = 0.491) [Figure 4.1 (b1)]. At t = 120 minutes, gait speed was not different from the baseline on the WW (108.74 ± 19.14cm/s, P = 0.367) or 'GW' (108.30 ± 24.70cm/s, P = 0.268) days.

Subjects without PPH. There was a no significant difference in gait speed over time between t = 0 - 120 minutes on the 'WW' (P = 0.327) or 'GW' (P = 0.216) days. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in gait speed from the baseline between the 'WW' and 'GW' days (95% CI = - 540 - 337, P = 0.617) [Figure 4.1 (b2)]. At t = 120 minutes, gait speed was not different from the baseline on the 'WW' (113.25 ± 26.22cm/s, P = 0.220) or 'GW' (110.25 ± 28.74cm/s, P = 0.590) days.

4.3.3 Stride length variability

Subjects with PPH. There was a significant increase (P = 0.028) in stride length variability over time between t = 0 - 120 minutes on the 'GW' day but there was no difference on the 'WW' day (P = 0.227). The mean maximum increase, and time of increase, in stride length variability were 0.27 ± 2.12cm at t = 69 ± 31 minutes. Between t = 0 – 120 minutes, there was no significant treatment effect for the AUC for the change in stride length variability from baseline between the 'WW' and 'GW' days (95% CI = - 102 - 46, P = 0.419) [Figure 4.1 (c1)]. At t = 120 minutes, there was a trend for stride length variability to be less than baseline on the 'WW' (3.00 ± 1.37cm, P = 0.090) but not the 'GW' (3.46 ± 1.23cm, P = 0.868) day.

Subjects without PPH. There was a significant decrease in stride length variability over time between t = 0 - 120 minutes on the 'WW' day (P = 0.008), but there was no difference on the 'GW' day (P = 0.593). The mean maximum decrease, and time of decrease, in stride length variability were 0.27 ± 1.89cm at t = 87 ± 37 minutes. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in stride length variability from the baseline between the 'WW' and 'GW' days (95% CI = - 54 - 122, P = 0.410) [Figure 4.1 (c2)]. At t = 120 minutes, stride length variability was not different from the baseline on the 'WW' (2.90 ± 1.27cm, P = 0.558) or 'GW' (3.35 ± 1.94cm, P = 0.858) days.

4.3.4 Double-support time variability

Subjects with PPH. There was a trend for a significant change (P = 0.073) in double-support time variability over time between t = 0 - 120 minutes on the 'GW' day, but there was no difference on the 'WW' (P = 0.261) day. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in double-support time variability from the baseline between the 'WW' and 'GW' days (95% CI = -1156 - 373, P = 0.287) [Figure 4.2 (a1)]. At t = 120 minutes, double-support time variability was not different from baseline on the 'WW' (11.24 ± 8.05s, P = 0.692) or 'GW' (13.37 ± 2.62s, P = 0.942) days.

Subjects without PPH. There was no significant change in double-support time variability over time between t = 0 - 120 minutes on the 'WW' (P = 0.297) or 'GW' (P = 0.203) days. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in double-support time variability from the baseline between the 'WW' and 'GW' days (95% CI = - 1283 - 569, P = 0.411) [Figure 4.2 (a2)]. At t = 120 minutes, double-support time variability was not significantly different than baseline on the 'WW' (20.27 ± 25.10s, P = 0.119) or 'GW' (17.82 ± 19.37s, P = 0.583) days.
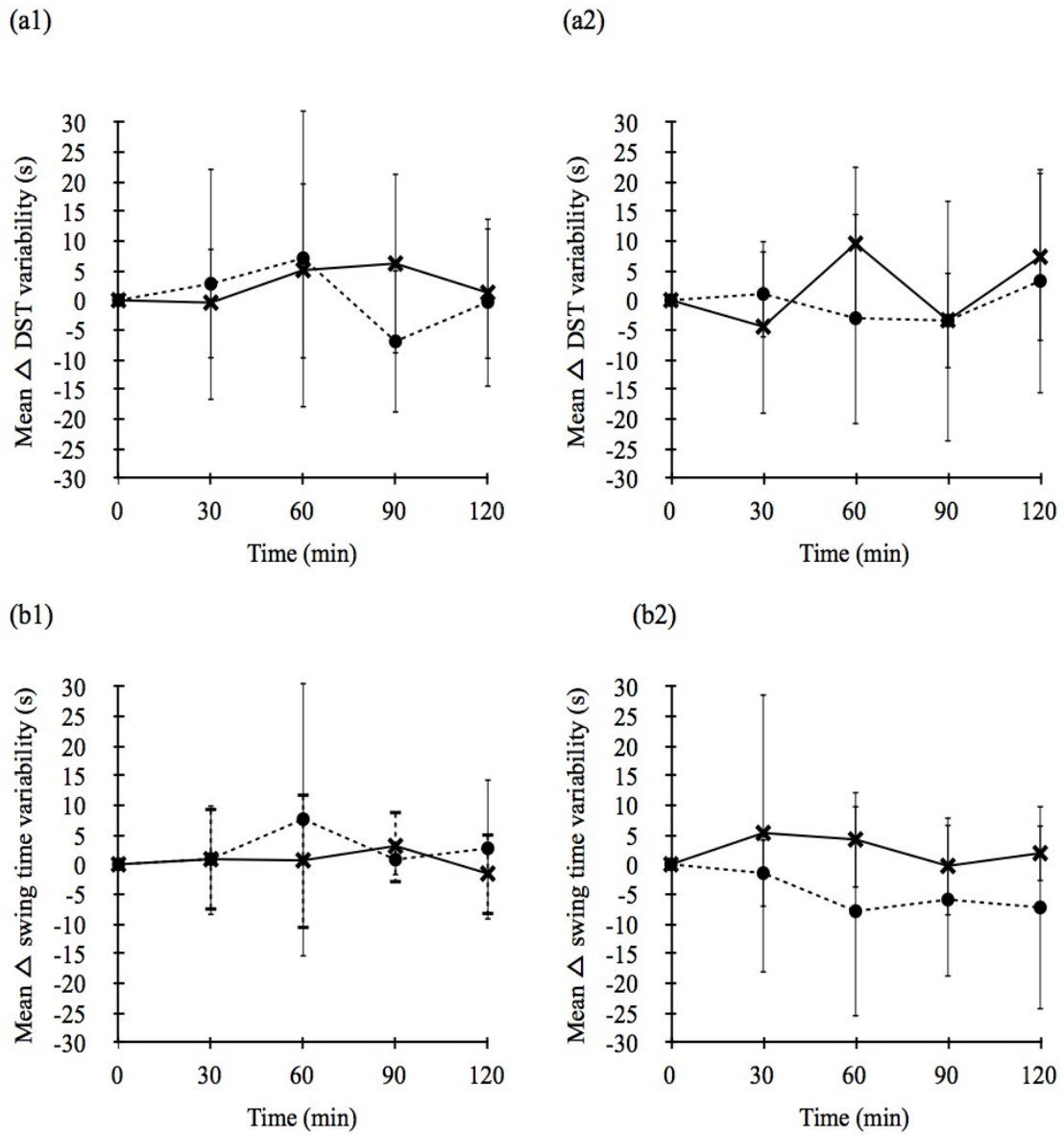
Mean change (△) in (a) double-support time (DST) variability and (b) swing time variability among (1) subjects with PPH and (2) without PPH on the 'WW' (×) and 'GW' (●) days. Data are mean values with standard deviation represented by vertical bars.

Figure 4.2   **Mean change in double-support time and swing time variability in subjects with and without PPH**

4.3.5 Swing time variability

Subjects with PPH. There was a trend for a significant increase (P = 0.073) in swing time variability over time between t = 0 - 120 minutes on the 'GW' day, but there was no difference on the 'WW' (P = 0.261) day. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in swing time variability from the baseline between the 'WW' and 'GW' days (95% CI = -347 - 755, P = 0.436) [Figure 4.2 (b1)]. At t = 120 minutes, swing time variability was not different from the baseline on the 'WW' (4.62 ± 4.51s, P = 0.438) or 'GW' (9.24 ± 9.56s, P = 0.434) days.

Subjects without PPH. There was no significant change in swing time variability between t = 0 - 120 minutes on the 'WW' (P = 0.193) or 'GW' (P = 0.538) days. Between t = 0 - 120 minutes, there was no significant treatment effect for the AUC for the change in swing time variability from the baseline between the 'WW' and 'GW' days (95% CI = - 6.57 - 1549, P = 0.052) [Figure 4.2 (b2)]. At t = 120 minutes, swing time variability was not different from the baseline on the 'WW' (7.88 ± 12.24s, P = 0.220) or 'GW' (4.94 ± 2.66s, P = 0.192) days.

4.4 Discussion

This is the first study to evaluate the effects of postprandial SBP decline on gait parameters in older individuals with and without PPH, especially gait parameter changes known to be associated with increased risk of falls; a decrease in gait speed; and an increase in the variability of stride length, double-support time and swing time (Dargent-Molina et al., 1996; Verghese et al., 2009; Callisaya et al., 2011). *The main findings of this study indicate that in older subjects with PPH, glucose ingestion significantly increases stride length variability, whilst in subjects without PPH, ingestion of water has the opposite effect, significantly decreasing stride length variability.*

The control of gait is a complex task that requires co-ordination between sensory, visual, vestibular, cerebellar, cognitive, psychological and musculoskeletal systems (Lord & Rochester, 2007). It has been suggested that in hypotensive states, the accompanying reduction in cerebral perfusion pressure may cause gait unsteadiness, potentially by affecting the vestibular, cerebellar and musculoskeletal systems (Barrett et al., 2008). Hence, this may be a possible mechanism by which PPH increases stride length variability.

Furthermore, there is evidence that hypotension is associated with poorer cognitive function, in particular, executive function (Frewen et al., 2014) which involves the ability to plan, sequence tasks and make judgements (Fuster, 1999). This reduction in function results from hypoperfusion of the prefrontal cortex, the area of the brain that controls executive function (Hayashida et al., 1996). Given that executive function plays a dominant role in the regulation of walking (Yogev-Seligmann et al., 2008; Hausdorff & Yogev, 2006), it is postulated that this may be another possible contributing factor to the changes in gait parameters in subjects with PPH noted in this study. In contrast to the increase in stride length variability among subjects with PPH after glucose ingestion, which is associated with increased falls risk, the decrease in the same parameter among subjects without PPH, following water ingestion, indicates a more steady gait (Barak et al., 2006) which may be as a result of the lack of hypotension and so, better cerebral perfusion on this day.

When considering the finding of this study, it is also interesting to note that in subjects with PPH, after glucose ingestion, the mean maximum fall in SBP occurred at ~ 70 minutes which coincides with the time that maximum changes in stride length variability become apparent. This observation supports the hypothesis that the accompanying hypotension may be the cause of detrimental gait changes.

While the strength of this study is that it specifically investigated the effects on gait parameters of glucose and water ingestion in older people with and without PPH, it is important to point out the limitations. Low-intensity intermittent walking has been suggested as a possible intervention to reduce the postprandial fall in SBP evident in people with PPH (Nair et al., 2015). Therefore, the walking protocol may have limited the potential influence on gait parameters and future research should consider this in its design. For example, the maximum change in gait was noted at the 60 minute mark and so it might be worthwhile undertaking an investigation to study the effect of glucose in subjects with PPH at the 60 minute mark only. However, it remains unknown whether prolonged sitting has an impact on gait measurements and this will also need to be considered in future study design.

In considering the findings of this study, it is very important to acknowledge that the number of subjects studied with PPH was less than the estimated power size required for adequate power. Therefore, care is needed when interpreting the trending results, especially trends. The recruitment

of the additional three subjects required for adequate power is ongoing and the results will be reanalysed and discussions amended accordingly to reflect any changed findings.

4.5   Conclusion

In conclusion, this study establishes for the first time that in older people with PPH, glucose ingestion increases stride length variability, a change known to be associated with increased falls risk (Verghese et al., 2009; Callisaya et al., 2011) in older people. This detrimental change to gait following glucose ingestion in subjects with PPH may be one mechanism contributing to the observed association of PPH with falls (Aronow & Ahn, 1994; Jansen et al., 1995; Le Couteur et al., 2003; Puisieux et al., 2000).

Chapter 5

Intermittent walking: A potential treatment for older people with postprandial hypotension

Summary

Exercise has been proposed as a possible treatment option for postprandial hypotension (PPH), (Jonsson et al., 1990; Oberman et al., 1999; Gentilcore et al., 2008c), yet its use has not been extensively investigated, as outlined in Chapter 2. This study was conducted to determine the effects of low-intensity, intermittent walking on the systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) responses to a 50 g glucose drink in older people with PPH.

The hypothesis was that low-intensity, repeated exercise would attenuate the hypotensive effects of a glucose drink in older people with PPH and that this effect would be sustained for the duration of the exercise.

Thirteen subjects with PPH were recruited and studied on two randomised days (control and intervention). On both study days, subjects ingested 200 ml of water containing 50 g glucose, followed by ambulatory BP and HR monitoring for 120 minutes. On the intervention day, subjects walked at their usual pace for 30 metres before the glucose drink and every 30 minutes following the glucose drink for 120 minutes. The results revealed that despite the significant decline in SBP on the control day, on the intervention day over the same period, there was no significant decline in SBP. Hence, this study suggests that in older people with PPH, intermittent walking at a usual pace commenced before a glucose drink and repeated every 30 minutes, attenuates the decline in SBP after the ingestion of a glucose drink. As a result of this research, intermittent walking may be recommended as a practical treatment strategy for older people with PPH.

This research forms the basis of a research paper peer reviewed and published in the *Journal of the American Medical Directors Association*, 2015 Feb 1;16(2):160-4 (Appendix 1).

5.1 Postprandial hypotension

Postprandial hypotension (PPH) is defined as a 20 mmHg reduction in SBP or a decline in SBP to less than 90 mmHg from a pre-ingestion SBP of greater than 100 mmHg, occurring within 120 minutes of meal commencement (Jansen & Lipsitz, 1995; Mathias et al., 1989). PPH occurs in older people, especially in those with autonomic dysfunction, most often due to diabetes (Jansen & Lipsitz, 1995) and Parkinson's disease (Chaudhuri et al., 1997). Prevalence rates ranging from 7% - 30% in healthy older people (Lipsitz & Fullerton, 1986), 24% - 57% in older nursing home residents (Aronow & Ahn, 1994; Le Couteur et al., 2003) and 24% - 91% among hospitalised older patients (Puisieux et al., 2000, Van Orshoven et al., 2010, Vloet et al., 2005) have been reported. Furthermore, PPH is more common than the more widely recognised orthostatic hypotension (Jansen & Lipsitz, 1995).

Symptoms of PPH range from lethargy, giddiness, dizziness to visual disturbance (Jansen & Lipsitz, 1995; Lipsitz & Fullerton, 1986) and PPH may lead to more significant consequences such as syncope, angina and cerebrovascular accidents (Vaitkevicius et al., 1991; Tabara et al., 2014). PPH has also been associated with falls in this group of individuals (Jansen & Lipsitz, 1995; Puisieux et al., 2000). Many older people experiencing PPH are asymptomatic (Van Orshoven et al.; 2010, Vloet et al., 2005), yet it has been recently demonstrated (Tabara et al., 2014) that negative consequences such as silent lacunar infarcts occur even in an asymptomatic group.

5.2 Attenuating postprandial fall in SBP in response to meals

Following the diagnosis of PPH, management options may include non-pharmacological and pharmacological strategies. Among the former, exercise has been proposed as a possible intervention (Jonsson et al. 1990; Oberman et al. 1999; Gentilcore et al. 2008c) to reduce the postprandial fall in SBP in response to a meal.

Jonsson et al. (1990). Jonsson et al. (1990) investigated the effects of a single walk at the subjects' usual pace for five minutes, 60 minutes following a standardised breakfast on SBP and heart rate (HR) among 58 older subjects living in a residential facility and 10 young healthy controls. Among the older group, 38 subjects (mean age 87 ± 6 years) were recurrent fallers, defined by two or more falls in the preceding six months, and 20 subjects were non-fallers (mean age 85 ± 4 years), defined by no falls in the preceding six months. The investigators reported that low-intensity walking exercise attenuated the postprandial hypotensive response to the meal by significantly increasing SBP and HR, however, this effect was not sustained upon cessation of the walking exercise.

Oberman et al. (1999). Subsequently, Oberman et al. (1999) reported that in 14 older people (mean age 88 ± 7 years) with PPH living in a residential facility, 10 minutes of low-intensity walking exercise, 20 minutes following completion of a breakfast meal, ameliorated the postprandial decline in mean arterial blood pressure with an associated increase in HR. However, like Jonsson et al. (1990), the investigators reported that this effect was only sustained for the duration of the exercise.

Gentilcore et al. (2008). More recently, Gentilcore et al. (2008) investigated the effects of high-intensity (ie 70% of the predicted maximum HR over 20 minutes) bicycle exercise on SBP and HR in ten healthy community dwelling older people (aged 67 - 79 years) following ingestion of a 300 ml glucose (75 g) drink. This intensity of exercise was demonstrated to exacerbate the hypotensive response to the glucose drink and accentuate the subsequent rise in HR; the effect on SBP was sustained until 180 minutes post drink ingestion (Gentilcore et al., 2008c).

A limitation of these previous studies is that postprandial exercise was conducted only a single time after a meal or after consuming a glucose drink. Hence, it remains unknown whether the observed effects of low-intensity exercise on postprandial SBP and HR will be sustained with low-intensity intermittent exercise commencing before a glucose drink.

Therefore, the aim of this study was to determine the effects of low-intensity intermittent walking on the SBP and HR responses to a 50 g glucose drink in older people with PPH. The broad hypothesis was that low-intensity, repeated exercise would attenuate the hypotensive effects of a glucose drink in older people with PPH and that this effect would be sustained for the duration of the exercise.

5.3   Methods

The protocol for this study was approved by the Human Research Ethics Committees of The Queen Elizabeth Hospital/Lyell McEwin Hospital/Modbury Hospital, Adelaide, Australia (protocol number 2011011). Each subject provided written, informed consent before the commencement of the first study day. All experiments were carried out in accordance with the Declaration of Helsinki.

5.3.1 Subjects

Thirteen older subjects (nine female, four male) with PPH were recruited from geriatrician clinics at The Queen Elizabeth Hospital, Adelaide, South Australia, or had previously participated in research studies conducted by the investigators. The mean age of the subjects was 76.5 ± 4 years (range 70 - 85 years). The studies were well tolerated with no adverse effects. No subject had a history of significant cardiovascular disease (myocardial infarction less than three months earlier, clinical coronary artery disease or symptomatic congestive heart failure), significant respiratory disease, renal impairment, epilepsy, dysphagia, chronic alcohol abuse or excessive cigarette smoking (more than10 cigarettes a day). Three subjects had orthostatic hypotension and of these, two also had definite autonomic dysfunction. Subjects withheld usual medication on the morning of the study days. All recruited subjects completed the study and no subject was symptomatic for giddiness, light-headedness, syncope or blurred vision. Subject characteristics are summarised in Table 5.1.

Table 5.1   Subject characteristics

Characteristic	Value
Age, years (mean ±SD*)	76.5 ± 4
Sex (n/ %)	
Male	4 (30.8)
Female	9 (69.2)
History of falls in preceding 12 months (n/%)	3 (23)
Orthostatic hypotension present (mean ± SD*)	3 (23.1)
SBP change (mmHg) (mean ± SD*)	-21.0 ± 9.5
DBP change (mmHg) (mean ± SD*)	6.3 ± 3.5
Autonomic nerve dysfunction score (mean ± SD*)	1.69 ± 0.85
Autonomic dysfunction present (n/%)	3 (23.1)
Charlson's Comorbidity Index (mean ± SD*)	2.07 ± 0.86
Hypertension (n/%)	7 (53.8)
Heart disease (n/%)	2 (15.4)
Diabetes Mellitus (n/%)	1 (7.7)
Hypothyroidism (n/%)	2 (15.4)
Beta blockers (n/%)	3
Calcium channel blockers-Dihydropiridines (n/%)	4
Calcium channel blockers-Non-Dihydropiridines (n/%)	0
ACE** inhibitors/ARB*** (n/%)	5
Diuretics (n/%)	2

* SD = Standard Deviation   ** ACE = Angiotensin Converting Enzyme   ***ARB = Angiotensin Receptor Blocker

5.3.2   Protocol

Each subject was studied on two occasions in a randomised order and each study day was separated by a minimum of 72 hours. The two study days were randomised using an online randomisation program (RANDOM.ORG, 1998). On both days, subjects underwent an overnight fast (10 hours for solids and 6 hours for liquids) and in the preceding 24 hours refrained from alcohol and caffeine containing beverages, and smoking for 12 hours.

Subjects attended the Basil Hetzel Institute at The Queen Elizabeth Hospital at 0830 hours on both days and upon arrival were seated comfortably in a chair and an automated blood pressure (BP) cuff was placed around the right arm for measurements of BP and HR (Visvanathan et al., 2005). Following a 10 minute rest period, at t = 0 minutes, subjects ingested a drink consisting of 50 g glucose (glucose monohydrate, Fluka Analytical, Sigma-Aldrich Pty Ltd, NSW, Australia) dissolved in water (total volume of the drink 200 ml). BP (systolic and diastolic) and HR were then measured for 120 minutes.

On the intervention day, subjects walked at their usual pace for a distance of 30 metres at t = - 20 minutes and then every 30 minutes between t = 30 - 120 minutes. On one day, cardiovascular autonomic nerve function and orthostatic BP were evaluated before the commencement of the study (Visvanathan et al., 2005).

5.3.3   Measurements

Blood pressure and heart rate. SBP, DBP and HR were measured using an automated oscillometric BP monitor (Spacelabs Ultralite 24 hour ABP, JLM Accutek Health Care, NSW, Australia). 'Baseline' BP and HR (t = 0 minutes) were calculated as the mean of measurements taken at t = -9, -6, and -3 minutes before ingestion of the drink. BP and HR were measured every 6 minutes between t = 0 - 60 minutes and then every 15 minutes between t = 60 - 120 minutes.

Cardiovascular autonomic function. Autonomic nerve function was assessed using standardised cardiovascular reflex tests (Ewing & Clarke, 1982; Piha, 1991). Parasympathetic function was determined by the variation (R-R interval) of HR during deep breathing and response to standing (30:15 ratio). Sympathetic function was assessed by the fall in SBP in response to standing. Each of the test results was scored according to age-adjusted predefined criteria as 0 = normal, 1 = borderline and 2 = abnormal for a total maximum score of 6. A score ≥3 was considered to indicate autonomic dysfunction (Ewing & Clarke, 1982; Piha, 1991).

5.3.4 Statistical analysis

Power calculations determined that to detect a mean change in SBP of 10 mmHg after oral glucose between study days (Visvanathan et al., 2005), a sample size of at least seven subjects was required to provide an 80% power, at the 0.05 significance level. SBP, DBP and HR were analysed as changes from baseline. One-way analysis of variance was used to analyse the effects of 'time' on SBP, DBP and HR. The maximum fall in SBP was defined as the greatest mean change from baseline in each subject at any given time point for each study day. Areas under the curve (AUC) between t = 0 - 120 minutes were calculated using the trapezoidal rule and analysed by one-way ANOVA to evaluate a 'treatment' effect for SBP, DBP and HR. All analyses were performed using SPSS Version 20 (SPSS Inc., Chicago, IL). Data are presented as means ± standard deviation. A P value < 0.05 was considered statistically significant in all analyses.

5.4 Results

There were no significant differences in baseline (t = 0 minutes) BP or HR between the study days (control vs. intervention):

  SBP: 148.69 ± 14.06 mmHg vs. 142.62 ± 14.16 mmHg, P = 0.07

  DBP: 75.46 ± 7.76 mmHg vs. 77.08 ± 8.40 mmHg, P = 0.35

  HR: 65.15 ± 7.86 bpm vs. 65.15 ± 8.45 bpm, P = 1.00

Systolic blood pressure. Between t = 0 - 120 minutes, there was a significant fall in SBP over time between t = 0 - 120 minutes on the control (P < 0.005) but not during the intervention (P = 0.520) day. The maximum fall in SBP was 18.7 ± 10.78 mmHg at t = 60 minutes. There was a significant treatment effect (P = 0.005) for the AUC for the change in SBP from baseline between the two study days (Figure 5.1a).

Diastolic blood pressure. Between t = 0 - 120 minutes, there was a significant fall in DBP over time on both the control (P = 0.016) and the intervention (P = 0.045) days. There was no significant treatment effect (P = 0.716) for the AUC for the change in DBP from baseline between the two study days (Figure 5.1b).

Heart rate. Between t = 0 - 120 minutes, there was no significant change in HR over time on either the control (P = 0.854) or intervention (P = 0.168) days. When three subjects taking beta-blocker medication were excluded from the analyses, there was still no significant change in HR over time on the study days (control: P = 0.196 vs. intervention: P = 0.500). There was also no significant treatment effect (P = 0.798) for the AUC for the change in HR from baseline between the two study days (Figure 5.1c).
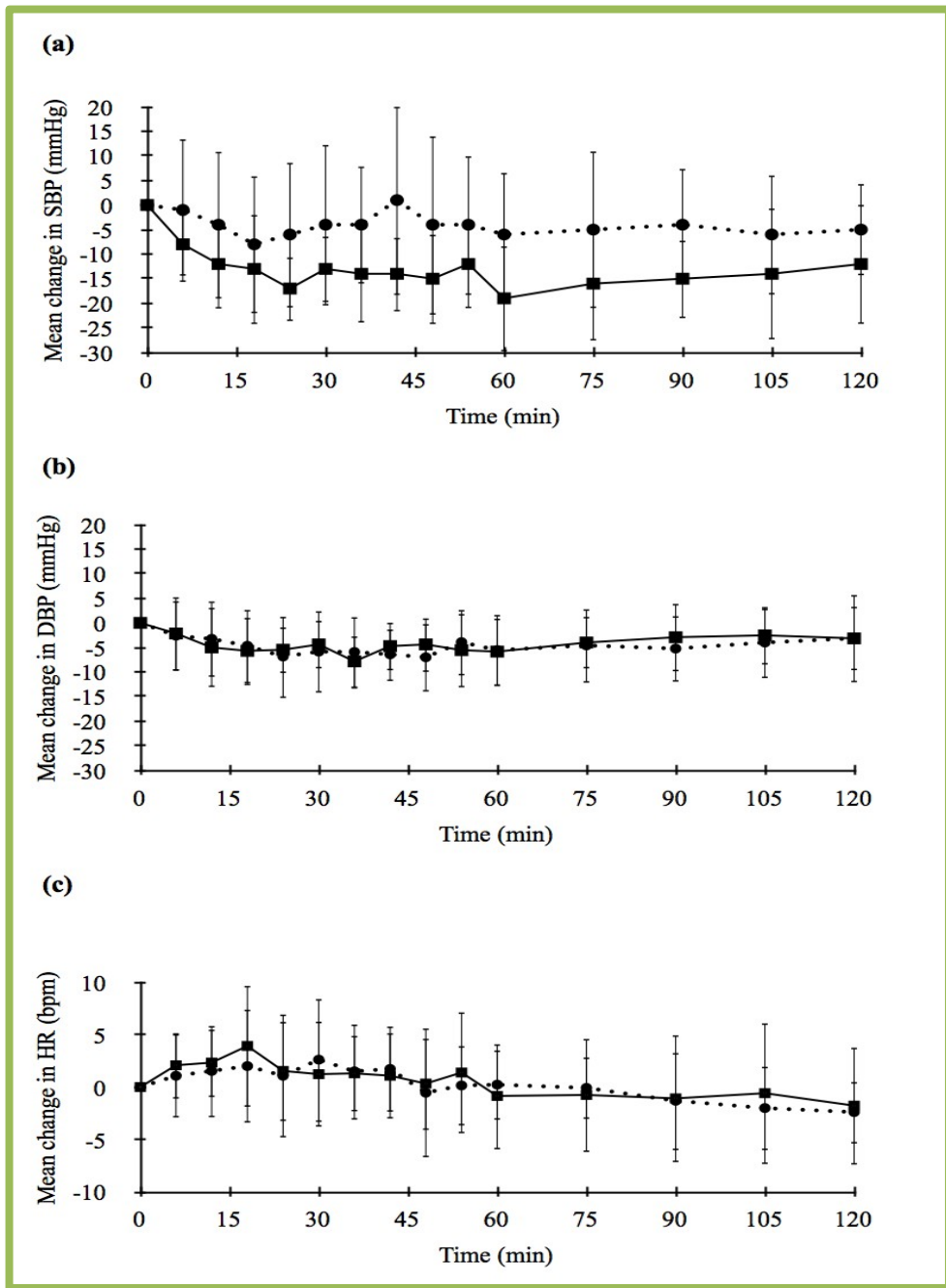
Figure 5.1(a, b, c)   Mean changes in a) SBP, b) DBP and c) HR from baseline on the control (glucose only) vs the intervention day (glucose and walking). Values are means for 13 subjects, with standard deviation represented by vertical bars.

5.5   Discussion

This study demonstrates that in older people with PPH:

- Low-intensity exercise in the form of intermittent walking commencing before the ingestion of a glucose drink significantly attenuates the systolic postprandial hypotensive response to the drink.

- This effect can be sustained for at least 120 minutes from drink ingestion commencement, the time period when PPH commonly occurs. These findings present a potential simple treatment strategy for older people who experience PPH.

Exercise after a meal has been previously proposed as a possible treatment strategy for PPH, although the demonstrated SBP attenuating effects lasted only as long as the exercise duration and with high-intensity exercise, the postprandial fall in SBP was exacerbated (Oberman et al., 1999).

As opposed to a single walking exercise regime occurring after meal ingestion, the current study differed in two ways from previously published research. Firstly, the exercise was instigated prior to a meal (glucose) ingestion and secondly, the exercise was intermittent; the latter probably a more realistic representation of the behaviour of individuals within two hours post meal commencement, intermittent walking to undertake different daily tasks.

SBP is influenced by cardiac output and total peripheral resistance; the former is a function of stroke volume and HR (Daida et al., 1996). The mechanism by which exercise may attenuate the postprandial fall in SBP is thought to reflect an augmentation of cardiac output during exercise (Fletcher et al., 2001).Vasoconstriction of the venous vasculature resulting in increased total peripheral resistance and redistribution of blood from the splanchnic circulation to exercising muscles contributes to an increased cardiac output (Fletcher et al., 2001). This leads to greater venous return and stroke volume resulting in increased SBP (Piha, 1991).

The rise in SBP demonstrated in the current study following walking exercise has been reported previously (Fletcher et al., 2001, Ogawa et al., 1992) in older people during acute exercise conditions. It has also been postulated that a rise in HR following exercise may also contribute to an increased SBP (Oberman et al., 1999); the former due to an initial withdrawal of vagal tone and a subsequent increase in sympathetic activity (Oberman et al., 1999). However, this physiological basis may not be a significant contributor to increasing SBP in this study, as there were no significant changes in HR following glucose induced hypotension and exercise.

The lack of HR increase noted in the current study has previously been described in other studies investigating PPH (Van Orshoven et al., 2010; Visvanathan et al., 2005; Lipsitz, 1983; Sivakumar & Soares, 2007), which suggest an additional mechanism at play contributing to the development of PPH. The most plausible explanation would be abnormalities in the baroreceptor function which may be impaired with ageing, particularly in hypertensive individuals (Ryan et al., 1992). In people with baroreceptor dysfunction, when BP declines, there is a failure of baroreceptor activation, hence, HR does not increase (Goldsmith et al., 1992).

Other possible contributing factors to the lack of a significant increase in HR in this study include the age-related decline in b-adrenergic responsiveness to sympathetic activation (Fletcher et al., 2001, Pan et al., 1986) and concomitant usage of beta blockers which act to inhibit a rise in HR (Pan et al., 1986). In this study, however, only two subjects were taking this medication regularly and when excluded from the analyses, there was still no significant change in HR over time on either study day, suggesting this is unlikely to be the probable reason for the lack of HR response to hypotension or low-intensity intermittent exercise.

Given people who exercise regularly exhibit a lower increase in HR during physical activity (Goldsmith et al., 1992) and that subjects in this study comprised relatively healthy older people residing in the community, this low-intensity intermittent walking exercise may not have been sufficiently challenging to exert a significant effect on HR, particularly in those people who participate in more intense exercise regularly.

In contrast to the diminished postprandial decline in SBP following exercise, the decline in DBP was not attenuated by low-intensity exercise, indicating that the postprandial diastolic effects of glucose could not be negated by intermittent walking. DBP is influenced primarily by total peripheral resistance and has been shown in the older person to increase to a smaller degree than SBP following exercise (Rowlands et al., 1984; McHam et al., 1999), remain unchanged or moderately decline following exercise (Fletcher et al., 2001). Therefore, our finding that DBP does not change over time after walking is not surprising.

The strengths of this study include that it investigated the role of low-intensity intermittent walking on postprandial BP specifically in older community dwelling people with PPH. This cohort has not

previously been evaluated. Low-intensity walking exercise was adopted in this group of subjects as it is widely accepted and achievable amongst a large number of older people, and can be incorporated into daily routine.

However, it is important to point out the limitations of this study:

- It was small and unblinded.

- Medications were withheld on the morning of the study day and may not accurately reflect daily life.

- The study concluded 120 minutes post drink ingestion commencement, therefore, it is uncertain if a decline in SBP would recur after this period.

- It remains to be seen if this intervention will have impact on important health outcomes such as falls risk.

5.6   Conclusion

In conclusion, this study establishes for the first time that in older people with PPH, low-intensity intermittent walking exercise at a usual pace attenuates the fall in SBP after ingestion of a glucose drink, an effect that can be sustained for at least 120 minutes from drink ingestion commencement. These observations support and encourage low-intensity walking exercise in the management of PPH.

Chapter 6

Neck of femur fractures within two hours of a meal

Summary

The study reported in this chapter sought to determine how commonly neck of femur (NOF) fractures occur following a fall within two hours of a meal, and the factors associated with the event. It was hypothesised that NOF fractures occurring within two hours of a meal could be related to PPH.

A prospective study was undertaken in the orthopaedic unit of a 320 bed general hospital. Consecutive first admissions of patients aged 70 years and over with fragility NOF fractures between March and November 2011 were included. Patients or their carers were interviewed using a standardised questionnaire. From the interviewees, 120 patients were recruited. The median age was 84.0 years. Falls within two hours of a meal occurred in 21% of patients. Patients who sustained a NOF fracture within two hours of a meal were more likely to be from residential care and experience symptoms associated with hypotension before the fall than patients who fell after more than two hours. Identification of the reasons for hypotension and potential management strategies would require further investigation.

This research forms the basis of a research paper peer reviewed and accepted for publication in the *Journal of Geriatrics and Gerontology Research* (Appendix 2).

6.1   Introduction

Falls occur frequently in older people, with a prevalence of 30% among community dwelling individuals and 50% among older people living in residential care facilities (Tinetti & Speechley, 1989). A major consequence of falls is fractures, which pose a considerable public health issue as they are associated with physical and psychological morbidity (Kannus et al., 1999; Rubenstein & Josephson, 2002), as well as significant health care costs (Moller, 2003). Over the past 50 years, the total number of fractures secondary to falls has increased worldwide, which is expected to continue (Kannus et al., 1999). In these circumstances, falls are already a critical issue and appear likely to pose a future challenge which it is crucial to address.

The implications for hip fractures, which are a third of all fractures, is particularly dismal, as reflected by a mortality of 10% - 28% at six months (Hannan et al., 2001), 33% mortality in the first year, permanent functional disabilities in 32% - 80% of cases (Magaziner et al., 1990; Jette et al., 1987) and institutionalisation in up to 35% of individuals who experience hip fracture (Johnell, 1997). Compared to other fractures, medical costs as a result of hip fractures are the highest, with estimates of costs of up to $5 billion dollars annually (Haentjens et al., 2005). Therefore, where a hip fracture can be prevented, it is important to do so.

Given that 90% of hip fractures in older people are a consequence of falls (Auron-Gomez & Michota, 2008), a key component of hip fracture prevention strategies requires the identification of risk factors associated with falls. The risk factors for falls in older people are typically multifactorial and the falls risk increases from 8% among those with no risk factors to 78% among those with four or more (Tinetti et al., 1988). Both orthostatic (Lipsitz, 1989; Rhebergen & Schölzel-Dorenbos, 2002) and postprandial hypotension (PPH) have been suggested as possible risk factors for falls (Tinetti et al., 1988; Aronow & Ahn, 1994; Le Couteur et al., 2003; Aronow & Ahn, 1997). PPH, as established earlier, is commonly defined as a 20 mmHg reduction in systolic blood pressure (BP) (Jansen et al., 1995) or a decline in systolic BP to less than 90 mmHg from a pre-ingestion pressure of greater than 100 mmHg within two hours of a meal (Mathias et al., 1989).

Although the fracture prevalence in older people according to the time of day (Norton et al., 1997, Formiga et al., 2008), there have been no studies reporting the prevalence of neck of femur (NOF) fractures as a result of a fall occurring within two hours of a meal. Therefore, the aim of the current research was to determine the prevalence of NOF fractures occurring within two hours of a meal, and the factors associated with these fractures, in older hospitalised patients.

6.2 Materials and methods

6.2.1 Participants

A prospective study of all overnight emergency patients aged 70 years and over, admitted to the orthopaedic unit of a 320 bed general teaching hospital in South Australia with NOF fractures following a low impact fall, was undertaken between March and November 2011. In this study, a low impact fall was defined as an unexpected event in which an older individual falls to the ground from an upper level or the same level as the individual. Approval for this study was provided by the Central Northern Adelaide Health Service Ethics for Human Research Committee (approval number: 2010178).

6.2.2 Protocol

Patients or their carers were interviewed within 72 hours of admission using a standardised questionnaire consisting of questions relating to demographic variables and the circumstances of the patient's fall. The time of the fracture in relation to meal ingestion was classified as either within two hours of a meal or longer. The time periods of the falls were categorised as 0000h-0600h, 0600h-1200h, 1200h-1800h, 1800h-2400h with the latter three time periods considered to correspond to breakfast, lunch and dinner, respectively.

A change in posture preceding a fall was considered relevant if the patient or carer reported that the patient had moved from either a supine to a sitting or standing position or from a sitting to a standing position. Patients were considered symptomatic of PPH before the fall if the following symptoms were reported: giddiness, light-headedness, syncope or blurred vision (Jansen & Lipsitz, 1995).

Global assessment of health status was assessed by calculating the Charlson Comorbidity Index (CCI), a measure of comorbidity, which predicts the one-year mortality rate for a patient by taking into account both the number and severity of 19 pre-defined comorbid conditions (Charlson et al., 1987). Each condition is assigned a score of 1, 2, 3 or 6, depending on the mortality risk associated with the condition. The scores are summed and a total score is derived. The one-year mortality rates for the different scores are: '0':12%; '1-2':26%; '3-4':52%; and 'greater than or equal to 5':85% (Charlson et al., 1987). Premorbid functional status was assessed using the Katz Index based on proxy reports and referenced to two weeks prior to admission (Folstein et al., 1975). The Katz Index assesses an individual's independence in performing six basic-care skills – feeding,

bathing, grooming, dressing, using the toilet and transferring between bed and chair. Each activity is scored '1' if independent and '0' if dependent in performing these tasks and the scores are summed. A score of '6' indicates full function, '4' indicates moderate impairment, and '2' or less indicates severe functional impairment (Katz et al., 1963).

Cognition was assessed by history of confusion and the Mini Mental State Examination (MMSE) (Folstein et al., 1975). The MMSE is a widely used screening instrument for measuring global cognitive status. The score is obtained from an aggregate of patient performance on questions that test orientation, memory, concentration, language, praxis, and visuoconstructional skills. Scores range from 0 to 30. Cognitive impairment is defined as either the mention of confusion in the medical records, a formal diagnosis of delirium, dementia or a MMSE of 24 or less.

6.2.3   Statistical analysis

Patients' characteristics were summarised using means and standard deviations, or frequencies and percentages, as appropriate. Comparisons between patient groups were performed using the chi-squared test and independent-samples t-test. One-sample chi-square testing was used to determine whether falls occurred randomly across the different time categories. Logistic regression analysis was performed to determine the independent associations of variables with fractures occurring within two hours of a meal. Variables associated with the outcome with a P value of less than 0.05 were entered into a multivariable logistic regression model and odds ratios with corresponding 95% confidence intervals were derived. The final model contained three independent variables – pre-admission residence, presence of symptoms, history of recurrent falls. All statistics were performed with the assistance of a professional biostatistician using *SPSS* statistical software, version 20 (SPSS Inc., Chicago, Illinois, USA).

6.3   Results

There were 138 admissions eligible for this study over the nine month study period, with 120 patients included in this study. Data from the remaining 18 patients were missing due to a shorter hospital admission duration or admission during holiday periods. There were no statistically significant differences between the included and the missed patients for age (included: 84.2 ± 7.5 years vs. missed: 85.7 ± 8.1 years; P=0. 452), gender (included: male 26.7% vs. missed: male 27.7%; P=0.921) and percentage admitted from their own home (included: 64.2% vs. missed: 66.6%; P=0.836).

Table 6.1 summarises the patients' characteristics and compares the overall group with those who fell within or after two hours of a meal. Generally, the patients in this study were considered very old with a mean age of 84.2 (± 7.5) years. In keeping with this age demographic, 73.3% of patients were female, 64.2% of patients were living at home prior to hospitalisation, while the remaining 35.8% of patients were from residential care. 32.5% of all falls were related to a change in posture. The possibility of cognitive impairment was noted in 57.5% of patients. In keeping with this, only 56.7% of patients provided a falls history themselves, while collaborative history was obtained from carers for 43.4% of patients.

Table 6.1 **Characteristics of patients admitted with neck of femur (NOF) fractures: overall patient characteristics comparing those who fell within and after two hours of a meal**

Variables	Total Population n = 120	Fractures occurring ≤ 2 hours after a meal n = 25	Fracture occurring ≥ 2 hours after a meal n = 95	P value
Age, years (Mean/SD)	84.2 (7.5)	83.3 (5.5)	84.4 (7.9)	0.384
Gender, n (%)				
Male	32 (26.7)	4 (16)	28 (29.5)	0.212
Female	88 (73.3)	21 (84)	67 (70.5)	
Preadmission residence, n (%)				
Home	77 (64.2)	10 (40)	67 (70.5)	0.005*
Residential care	43 (35.8)	15 (60)	28 (29.5)	
Time of fracture, n (%)				
0600-1200	41 (34.2)	11 (44)	30 (31.6)	0.224^
1200-1800	36 (30)	8 (32)	28 (29.5)	
1800-2400	30 (25)	6 (24)	24 (25.2)	
0000-0600	13 (10.8)	0 (0)	13 (13.7)	
Source of history, n (%)				
Patient	68 (56.7)	15 (60)	53 (55.8)	0.705
Carer	52 (43.3)	10 (40)	42 (44.2)	
Change in posture preceding fall, n (%)	39 (32.5)	9 (36)	30 (31.6)	0.903
Hypotensive symptoms prior to fall (giddiness, light-headedness, syncope or blurred vision), n (%)	12 (10.0)	6 (24)	6 (6.3)	0.032*
Number of medications (Mean /SD)	5.8 (3.2)	6.3 (3.6)	5.6 (3.1)	0.35
> 1 fall in preceding 12 months, n (%)	65 (54.2)	18 (72)	47 (49.5)	0.044*
CCI, (Mean/SD)	2.4 (1.9)	2.2 (2.0)	2.4 (1.9)	0.648
Heart Disease, n(%)	64 (53.3)	11	53	0.293
Hypertension, n (%)	76 (63.3)	15	61	0.697
Diabetes Mellitus, n (%)	30 (25)	6	24	0.897
MMSE, (Mean/SD)	20.1(8.4)	20.3 (9.2)	20.0 (8.2)	0.9
Katz Index, (Mean/SD)	3.9 (2.2)	3.2 (2.4)	4.1 (2.2)	0.08

Overall, there was a statistically significant difference (P=0.002) between the proportion of total falls occurring in the four time categories, with the lowest percentage of falls occurring at night – 10.8% between 0000h-0600h. Over the other time periods of falls, 34.2% of falls occurred between 0600h-1200h (following breakfast), 30% between 1200h-1800h (following lunch), and 25% occurred between 1800h-2400h (following dinner).

In the current study, 20.8% of NOF fractures occurred within, and 79.2% after, two hours of meal ingestion. NOF fractures as a result of a fall occurring within two hours of a meal occurred among 34.8% of patients in residential care and 13.0% of patients living in their own homes (P=0.009). One or more falls in the preceding 12 months occurred among 72% of patients who sustained a fall within, compared to 49.5% after, two hours of meal ingestion (P=0.044). Symptoms of hypotension (giddiness, light-headedness, syncope or blurred vision) prior to the fall were reported more commonly (24.0%) by patients who fell within two hours of a meal when compared with those (6.3%) who fell after more than two hours (P=0.032). The percentage of participants who changed posture prior to a fall was similar – 36% for those falling within two hours; 31.6% for those falling after a two hour period (P=0.903).

In the logistic regression model, factors found to be independently associated with NOF fractures occurring within two hours of a meal were being in residential care (OR 3.0, CI 1.009-8.687; P=0.048) and experiencing symptoms associated with hypotension prior to the fall (OR 5.2, CI 1.342-20.129; P=0.017). There were no significant differences between the two groups for all other variables.

6.4   Discussion

Among older patients admitted with NOF fractures, one-fifth of fractures occurred within two hours of a meal. The majority of NOF fractures occurred during the day with only a small percentage occurring at night. Furthermore, compared with study patients who sustained a NOF fracture after more than two hours had passed, patients who sustained NOF fractures within two hours of a meal were more likely to be living in residential care, to have experienced symptoms associated with hypotension before a fall and have a history of recurrent falls in the preceding 12 months.

The distribution of falls across the four time categories in the current research indicated that the least number of falls occurred at night. This is consistent with previous research, such as that by Norton et al. (1997), who found that 10.4% of falls among patients with a NOF fracture occurred at night. More falls occurred during the day, most likely due to increased ambulation in the daylight hours, which is desirable to maintain physical independence (Lehtola et al., 2006; Overstall, 1992).

The significantly higher proportion of older patients from residential care who sustained NOF fractures within two hours of meal ingestion may be attributed to underlying differences in co-morbidities that affect the risk of falling following a meal. PPH would be one such co-morbidity in view of the accompanying BP changes that occur after a meal. Furthermore, a higher PPH prevalence has been reported among older people in residential care (24%-57%) (Aronow & Ahn, 1994; Le Couteur et al., 2003; Vaitkevicius et al., 1991) compared to those at home (7%-30%) (Lipsitz & Fullerton, 1986).

Patients sustaining a NOF fracture within two hours of a meal were more likely to report symptoms consistent with hypotension compared to those falling after two hours had passed. The absence of a significant difference in change in posture before the fall between the two groups of patients suggests that orthostatic hypotension is less likely to be a contributing factor. It can be speculated that the hypotensive symptoms may be related to PPH. We, therefore, suggest that older people presenting with falls might benefit from being assessed for symptoms of hypotension occurring within two hours of a meal, as when PPH is diagnosed there are a range of simple non-pharmacological strategies for its management.

For example, drinking water before a meal (Deguchi et al., 2007; Jones et al., 2005) and dietary modification, such as consuming smaller portions of meals more frequently and avoiding excessive carbohydrate intake (Puvi-Rajasingham & Mathias, 1996) can reduce the occurrence of PPH, thus reducing the risk of falls and possibly, fractures. However, before firm conclusions can be drawn, there is a need to further investigate this theory by undertaking research involving the systematic measurement of blood pressure.

A history of recurrent falls in the preceding 12 months, which was significantly more common among older patients who sustained NOF fractures within two hours of a meal, may be attributed to

the presence of factors that increase the falls risk in this group. The fact that there was no significant difference in the mean Charlson Comorbidity Index between older patients who sustained NOF fractures within or after two hours of a meal, suggests the presence of co-morbidities that the Charlson Comorbidity Index does not capture.

In considering the observations of the research, it should be understood that cognitive impairment was present in over half of the patients and so there may be inaccuracies pertaining to the actual time of the fall reported in some patients. Furthermore, broad time categories were used to symbolise breakfast, lunch and dinner rather than specifically clarifying when patients had ingested their last meals. This surrogate history measure for PPH was considered more logistically feasible in this population group and was, therefore, employed rather than the more objective evaluation of BP reduction following a meal. The generalisability of the findings of this study is restricted and future research should consider all patients admitted overnight who have experienced a fall.

In conclusion, in this prospective study, 20.8% of NOF fractures occurred within two hours of a meal. Patients who sustained a NOF fracture within two hours of a meal were more likely to be living in residential care, experience symptoms associated with hypotension before the fall and have a history of recurrent falls in the preceding 12 months compared with patients who experienced a fall after two hours of a meal. PPH may be a contributing factor in this group of patients, therefore, patients who present with falls and symptoms of hypotension within two hours of a meal could be further investigated for PPH. Where PPH is diagnosed, simple non-pharmacological strategies may be recommended.

Chapter 7

Conclusion

PPH is common among older people in the community, residential care and hospitals (Jansen & Lipsitz, 1995). It is associated with numerous adverse outcomes, one of which is falls (Jansen & Lipsitz, 1995; Puisieux et al., 2000), which itself results in devastating consequences particularly fractures. As Australia is experiencing an expanding ageing population (ABS, 2008), PPH will become increasingly prevalent hence there is a need to tackle this issue. However before this can be undertaken effectively, there are aspects of PPH which need to be explored further and these areas are covered in this thesis.

Current management strategies for PPH are sub-optimal. Non-pharmacological strategies have not been specifically evaluated in older people with PPH and available options may not be widely applicable, whereas pharmacological strategies have potential adverse effects (Chiasson et al., 2003). The role of exercise in treating PPH has not been extensively investigated. This aspect was explored in Chapter 5, where among community dwelling older people with PPH, it was demonstrated for the first time that intermittent walking for a short distance, commencing before a glucose drink and repeated at 30 minute intervals, was demonstrated to attenuate the postprandial decline in systolic BP, an effect that was sustained for at least 120 minutes after the beginning of drink ingestion (Nair et al., 2015). This could potentially ameliorate any negative consequences of PPH, including falls. Furthermore, as this level of low intensity intermittent exercise would be practical among a wide range of older people, this presents a therapeutic option which would be clinically relevant. In addition, in view that exercise has multiple other health benefits (Miller et al., 2000), this renders exercise all the more meaningful as a possible therapeutic option.

The risk factors for falls in older people are typically multifactorial and it is essential to identify all falls risk factors (Tinetti et al., 1988; Stevens 2005; Tromp et al., 2001). PPH and gait impairments are examples of two risk factors relevant to falls prevention (Tan & Kenny, 2006; Tinetti et al., 1988; Rubenstein, 2006). Although the association between falls and PPH has been established (Jansen & Lipsitz, 1995; Puisieux et al., 2000), it is uncertain if this occurs through detrimental effects on gait, as this has not yet been investigated. This was the aim of the study described in Chapter 4. In this novel study to evaluate the effects of postprandial decline in systolic BP on gait

parameters among community dwelling older people, among subjects with PPH, following glucose ingestion, there was a significant increase in stride length variability. Increased variability in stride length has been shown to predict future risk of falls and injurious falls specifically (Verghese et al., 2009, Callisaya et al., 2011). Therefore the effect of postprandial systolic BP decline among subjects with PPH seen in this study is clinically relevant. There was a lack of significant detrimental change in stride length variability among subjects without PPH following glucose which is indicative that the accompanying systolic BP decline that occurs among subjects with PPH following glucose contributed to the detrimental gait changes.

The main aim of falls prevention strategies are to reduce fractures as this is the most detrimental consequence of falls (Sattin et al., 1990; Rubenstein & Josephson, 2002). However, not all falls result in fractures and despite the studies exploring the relationship between PPH and falls, there are no studies evaluating the association between PPH and fractures. Chapter 6 explores this in an exploratory study to determine the prevalence of neck of femur fractures that occur within two hours of a meal and the factors independently associated with this among older hospitalised patients. Falls within two hours of a meal occurred in 20.8% of patients and independent factors associated with falls occurring within two hours of a meal were symptoms of hypotension prior to a fall and being in residential care (Nair et al., 2014). Therefore patients with symptoms of hypotension within two hours of a meal and a history of falls could be formally investigated for postprandial hypotension.

The results of this thesis have contributed to providing evidence for the first time that intermittent walking exercise is an effective and practical therapeutic option for older people with PPH. The second contribution was demonstrating the detrimental effects of postprandial BP decline on stride length variability, which assist in understanding the relationship between PPH, gait impairments and falls. The third contribution was identifying the prevalence of fractures occurring within two hours of a meal and factors associated with this, thus emphasising that this cohort of patients need to be further investigated for the presence of PPH so that this can be addressed appropriately with the potential of preventing further fractures.

The research presented in this thesis creates opportunities for future research possibilities:

- Arising from the study described in Chapter 4, a redesign of the walking protocol to ensure that gait analysis is only undertaken once each study day to eliminate the mitigating effects of walking itself on BP and evaluating the impact of prolonged sitting on gait measurements in older people.

- From the results of Chapter 5, evaluating the effect of similar exercise on SBP beyond 120 minutes as it is uncertain if a decline in SBP would recur after this period and appraising if the exercise intervention will have impact on health outcomes such as falls risk. In addition, the lack of a significant increase in heart rate among subjects with PPH even following exercise, warrants further investigation.

- Finally, the results from Chapter 6, patients who present with falls and symptoms of hypotension within two hours of a meal could be further investigated for PPH thereby providing a targeted approach in measuring the prevalence of PPH among hospitalised older people.

In conclusion, this thesis provides evidence for an effective therapeutic option for older people with PPH, insight into the possible mechanism by which postprandial SBP decline affects gait detrimentally and reports the timing of neck of femur fractures occurring within two hours of a meal.

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Appendices

Appendix 1   Statement of authorship and published paper:
Chapter 5 Intermittent Walking: A Potential Treatment for Older
People with Postprandial Hypotension

Appendix 2   Statement of authorship and accepted paper:
Chapter 6 Neck of femur fractures within two hours of a meal

Appendix 3   Oral abstracts/ Platform presentations

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Neck of Femur Fractures within Two Hours of a Meal

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Abstract

Aim: To determine in older hospitalized patients the prevalence of neck of femur (NOF) fractures occurring within two hours of a meal and the factors associated with these fractures.

Methods: A prospective study was undertaken within the orthopedic unit of a 320 bed general hospital. Consecutive first admissions of patients aged 70 years and over with fragility NOF fractures between March and November 2011 were included. Patients or their careers were interviewed using a standardised questionnaire.

Results: 120 patients were recruited. The median age was 84.0 years. Falls within two hours of a meal occurred in 20.8% of patients. Independent factors associated with falls occurring within two hours of a meal were symptoms of hypotension prior to a fall (OR 5.2, CI 1.342-20.129; P=0.017) and being in residential care (OR 3.0, CI 1.009-8.687; P=0.048).

Conclusion: Patients who sustained a NOF fracture within two hours of a meal were more likely to be from residential care and experience symptoms associated with hypotension before the fall compared with patients who experienced a fall after two hours of a meal; identification of the reasons for hypotension and potential management strategies require further investigation.

Keywords: Aging; Blood pressure; Fractures; Hypotension; Postprandial

Introduction

Falls occur frequently in older people, with a prevalence of 30% among community dwelling individuals and 50% among older people living in residential care facilities [1]. A major consequence of falls is fractures which pose a considerable public health issue as they are associated with detrimental physical and psychological morbidity [2,3] as well significant health care costs [4]. Given that there has been a worldwide increase in the total number of fractures secondary to falls over the past 50 years which is projected to continue [2], falls appear likely to pose a future challenge which is crucial to address. The implications for hip fractures which occur among a third of all fractures is particularly dismal as reflected by a mortality of 10%-28% at six months [5], 33% mortality in the first year, permanent functional disabilities in 32%-80% [6,7] and institutionalization in up to 35% of individuals [8]. Compared to other fractures, medical costs as a result of hip fractures are the highest with estimates of costing $5 billion dollars annually [9]. Therefore, where a hip fracture can be prevented, it is important to do so.

Given that 90% of hip fractures in older people are a consequence of falls [10], a key component of hip fracture prevention strategies requires the identification of risk factors associated with falls. The risk factors for falls in older people are typically multifactorial and the falls risk increases from 8% among those with no risk factors to 78% among those with four or more risk factors [11]. Both orthostatic [12,13] and postprandial hypotension (PPH) have been suggested to be possible risk factors for falls [11,14-16]; the latter is defined commonly as a 20 mmHg reduction in systolic blood pressure (BP) [17] or a decline in systolic BP to less than 90 mmHg from a pre-ingestion pressure of greater than 100 mmHg within two hours of a meal [18].

Although the fracture prevalence in older people according to the time of day has been previously published [19,20], there have been no studies reporting the prevalence of neck of femur (NOF) fractures as a result of a fall occurring within two hours of a meal. Therefore, the aim of this study was to determine in older hospitalized patients the prevalence of NOF fractures occurring within two hours of a meal and the factors associated with these fractures.

Materials and Methods

Participants

A prospective study of all overnight emergency patients aged 70 years and over, admitted to the orthopedic unit of a 320 bed general teaching hospital in South Australia with NOF fractures following a low impact fall, was undertaken between March and November 2011. In this study, a low impact fall was defined as an unexpected event in which an older individual falls to the ground from an upper level or the same level as the individual. Approval for this study was provided by the Central Northern Adelaide Health Service Ethics for Human Research Committee (approval number: 2010178).

Protocol

Patients or their carers were interviewed using a standardized questionnaire consisting of questions relating to demographic variables and the circumstances of the patient's fall within 72 hours of admission. The time of the fracture in relation to meal ingestion was classified as either within two hours of a meal or longer. The time periods of the falls were categorised as 0000-0600 h, 0600-1200 h, 1200-1800 h, 1800-2400 h with the latter three time periods considered to correspond to breakfast, lunch and dinner, respectively. In this study, a change in posture preceding a fall was considered relevant if the patient or carer reported that the patient had transferred from either a supine to sitting or standing position or from a sitting to standing position. Patients were considered symptomatic of PPH before the fall if the following symptoms were reported: giddiness, light-headedness, syncope or blurred vision [21]. Global assessment of health status was assessed by calculating the Charlson Comorbidity Index (CCI), a measure of comorbidity, which predicts the one-year mortality rate for a patient by taking into account both the number and severity of 19 pre-defined comorbid conditions [22]. Each condition is assigned a score of 1, 2, 3 or 6 depending on the mortality risk associated with the condition. The scores are summed and a total score is derived. The one-year mortality rates for the different scores are: '0':12%; '1-2':26%; '3-4':52%; and 'greater than or equal to 5':85% [22]. Premorbid functional status was assessed using the Katz Index based on proxy reports and referenced to two weeks prior to admission [23]. The Katz Index assesses an individual's independence in performing six basic-care skills (feeding, bathing, grooming, dressing, using the toilet and transferring between bed and chair). Each activity is scored '1' if independent and '0' if dependent in performing these tasks and the scores are summed. A score of 6 indicates full function, 4 indicates moderate impairment, and 2 or less indicates severe functional impairment [24]. Cognition was assessed by history of confusion and the Mini Mental State Examination (MMSE) [23]. The MMSE is a widely used screening instrument for measuring global cognitive status. The score is obtained from an aggregate of patient performance on questions around orientation, memory, concentration, language, praxis, and visuoconstructional skills. Scores range from 0 to 30. Cognitive impairment is defined as either the mention of confusion in the medical records, a formal diagnosis of delirium, dementia or a MMSE of 24 or less.

Statistical analysis

Patients' characteristics were summarized using means and standard deviations, or frequencies and percentages, as appropriate. Comparisons between patient groups were performed using the chi-squared test and independent-samples t-test. One-sample chi-square test was used to determine if falls occurred randomly across the different time categories. Logistic regression analysis was performed to determine the independent associations of variables with fractures occurring within two hours of a meal. Variables associated with the outcome with a P value less than 0.05 were entered into a multivariable logistic regression model and odds ratios with corresponding 95% confidence intervals were derived. The final model contained three independent variables (pre-admission residence, presence of symptoms, history of recurrent falls). All statistics were performed with the assistance of a professional biostatistician using SPSS statistical software, version 20 (SPSS Inc., Chicago, Illinois, USA).

Results

There were a total of 138 admissions eligible for this study over the nine month study period with 120 patients included in this study. Data from the remaining 18 patients were missing due to a shorter hospital admission duration or admission during holiday periods. There were no statistically significant differences between the included and the missed patients for age (included: 84.2±7.5 years vs. missed: 85.7±8.1 years; P=0. 452), gender (included: male 26.7% vs. missed: male 27.7%; P=0.921) and percentage admitted from their own home (included: 64.2% vs. missed: 66.6%; P=0.836).

Table 1 summarizes the patients' characteristics and compares the overall group with those who fell within and after two hours of a meal. Generally, the patients in this study were considered very old with a mean age of 84.2 (±7.5) years. In keeping with this age demographic, 73.3% of patients were female, 64.2% of patients were living at home prior to hospitalization while the remaining 35.8% of patients were from residential care. 32.5% of all falls were related to a change in posture. The possibility of cognitive impairment was noted in 57.5% of patients. In keeping with this, only 56.7% of patients provided a falls history themselves while collaborative history was obtained from carers for 43.4% of patients.

Variables	Total Population n = 120	Fractures occurring≤2 hours after a meal n = 25	Fracture occurring >2 hours after a meal n = 95	P value
Age, years (Mean/SD)	84.2 (7.5)	83.3 (5.5)	84.4 (7.9)	0.384
Gender, n (%)				
Male	32 (26.7)	4 (16)	28 (29.5)	0.212
Female	88 (73.3)	21 (84)	67 (70.5)	
Preadmission residence, n (%)				
Home	77 (64.2)	10 (40)	67 (70.5)	0.005*
Residential care	43 (35.8)	15 (60)	28 (29.5)	
Time of fracture, n (%)				
0600-1200	41 (34.2)	11 (44)	30 (31.6)	0.224^
1200-1800	36 (30)	8 (32)	28 (29.5)	

1800-2400	30 (25)	6 (24)	24 (25.2)	
0000-0600	13 (10.8)	0 (0)	13 (13.7)	
Source of history, n (%)				
Patient	68 (56.7)	15 (60)	53 (55.8)	0.705
Carer	52 (43.3)	10 (40)	42 (44.2)	
Change in posture preceding fall, n (%)	39 (32.5)	9 (36)	30 (31.6)	0.903
Hypotensive symptoms prior to fall (giddiness, light-headedness, syncope or blurred vision), n (%)	12 (10.0)	6 (24)	6 (6.3)	0.032*
Number of medications (Mean /SD)	5.8 (3.2)	6.3 (3.6)	5.6 (3.1)	0.35
≥ 1 fall in preceding 12 months, n (%)	65 (54.2)	18 (72)	47 (49.5)	0.044*
CCI, (Mean/SD)	2.4 (1.9)	2.2 (2.0)	2.4 (1.9)	0.648
Heart Disease, n (%)	64 (53.3)	11	53	0.293
Hypertension, n (%)	76 (63.3)	15	61	0.697
Diabetes Mellitus, n (%)	30 (25)	6	24	0.897
MMSE, (Mean/SD)	20.1(8.4)	20.3 (9.2)	20.0 (8.2)	0.9
Katz Index, (Mean/SD)	3.9 (2.2)	3.2 (2.4)	4.1 (2.2)	0.08

Table 1: Characteristics of patients admitted with neck of femur (NOF) fractures: overall patient characteristics comparing those who fell within and after two hours of a meal. *<0.005 significant, ^chi-squared test between patients who fell within and after two hours of a meal.

Overall, there was a statistically significant difference (P=0.002) between the proportion of total falls occurring in the four time categories with the lowest percentage of falls occurring at night, 10.8% between 0000-0600 h. Over the other time periods of falls, 34.2% of falls occurred between 0600-1200 h (following breakfast), 30% between 1200-1800 h (following lunch), and 25% occurred between 1800-2400 h (following dinner).

In this study, 20.8% of NOF fractures occurred within, and 79.2% after, two hours of meal ingestion. NOF fractures as a result of a fall occurring within two hours of a meal occurred among 34.8% of patients from residential care and 13.0% of patients from their own home (P=0.009). One or more falls in the preceding 12 months occurred among 72% of patients who sustained a fall within, compared to 49.5% after, two hours of meal ingestion (P=0.044). Symptoms of hypotension (giddiness, light-headedness, syncope or blurred vision) prior to the fall were reported more commonly (24.0%) by patients who fell within two hours of a meal when compared with those (6.3%) who fell after two hours of a meal (P=0.032). A change in posture prior to a fall was similar between those patients who fell within, and after two hours of a meal (36% and 31.6%, respectively (P = 0.903)).

In the logistic regression model, factors found to be independently associated with NOF fractures occurring within two hours of a meal were being in residential care (OR 3.0, CI 1.009-8.687; P=0.048) and experiencing symptoms associated with hypotension prior to the fall (OR 5.2,CI1.342-20.129;P=0.017). There were no significant differences between the two groups for all other variables.

Discussion

Among older patients admitted with NOF fractures, one-fifth of fractures occurred within two hours of a meal. The majority of NOF fractures occurred during the day with only a small percentage occurring during the night. Also, patients who sustained a NOF fracture within two hours of a meal were more likely to be from residential care, experience symptoms associated with hypotension before a fall and had a history of recurrent falls in the preceding 12 months compared with patients who experienced a fall after two hours of a meal.

The overall distribution of falls across the four time categories was significantly different with the lowest prevalence of falls occurring at night. This is consistent with previous research indicating that injurious falls were more likely to occur during the day and is believed to be related to increased ambulation, which is desirable to maintain physical independence [25,26]. It has also previously been reported by Norton et al. [19] that 10.4% of falls among patients admitted with a fractured femur occurred at night, consistent with our finding.

The significantly higher proportion of older patients from residential care who sustained NOF fractures within two hours of meal ingestion compared to older patients living at home, may be attributed to underlying differences in co-morbidities that affects the risk of falling following a meal. PPH would be one such co-morbidity in view of the accompanying BP changes that occur after a meal. Furthermore, a higher PPH prevalence has been reported among older people in residential care (24%-57%) [14,15,27] compared to those at home (7%-30%) [28].

Patients sustaining a NOF fracture within two hours of a meal were more likely to report symptoms consistent with hypotension

compared to those falling after two hours of a meal. The absence of a significant difference in change in posture before the fall, between the two groups of patients, may suggest that orthostatic hypotension is less likely to be a contributing factor. It can be speculated that the hypotensive symptoms may be related to PPH. We, therefore, suggest that older people presenting with falls might benefit from being assessed for symptoms of hypotension occurring within two hours of a meal as when PPH is diagnosed, there are a range of simple non-pharmacological strategies for the management of PPH that could be recommended. For example, drinking water before a meal [29,30] and dietary modification such as consuming smaller portions of meals more frequently and avoiding excessive carbohydrate intake [31]. This may reduce the risk of PPH and, hence, falls and possible fractures. However, before firm conclusions can be drawn, there is a need to further investigate this theory by undertaking research whereby measurement of blood pressure is undertaken.

A history of recurrent falls in the preceding 12 months, which was significantly more common among older patients who sustained NOF fractures within two hours of a meal, may be attributed to the presence of factors that increase the falls risk in this group. In view that there was no significant difference in the mean Charlson Comorbidity Index between older patients who sustained NOF fractures within and after two hours of a meal, this suggests the presence of co-morbidities that the Charlson Comorbidity Index does not capture.

In considering our observations, it should be recognized that cognitive impairment was present in patients and so there may be inaccuracies pertaining to the actual time of the fall reported in some patients. Furthermore, broad time categories were used to symbolize breakfast, lunch and dinner rather than specifically clarifying when patients had ingested their last meals. This surrogate history measure for PPH was considered more logistically feasible in this population group and was, therefore, employed rather than the more objective evaluation of BP reduction following a meal. The generalizability of the findings of this study is restricted and future research should consider all patients admitted overnight who have experienced a fall.

In conclusion, in this prospective exploratory study, 20.8% of NOF fractures occurred within two hours of a meal. Patients who sustained a NOF fracture within two hours of a meal were more likely to be from residential care, experience symptoms associated with hypotension before the fall and had a history of recurrent falls in the preceding 12 months compared with patients who experienced a fall after two hours of a meal. PPH may be a contributing factor in this group of patients, therefore, patients who present with falls and symptoms of hypotension within two hours of a meal could be further investigated for PPH. Where PPH is diagnosed, simple non-pharmacological strategies may be recommended.

Acknowledgments

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Appendix 3

Oral abstracts/ Platform presentations

'The effects of a postprandial blood pressure decline following a glucose drink on gait parameters in healthy older volunteers'. Oral presentation at the Australia and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting in Sydney, 2012.

'Intermittent Walking: A Potential Treatment Strategy for Older People with Postprandial Hypotension'. Oral presentation at the Australia and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting in Adelaide, South Australia, 2013.

'Is Postprandial Hypotension A Possible Contributor to Hip Fractures in Older People' at the Basil Hetzel Institute and The Queen Elizabeth Research Day, 2013.

'The postprandial blood pressure decline following a glucose drink affects gait detrimentally in older people' at the Basil Hetzel Institute and The Queen Elizabeth Research Day, 2014.

The effects of a postprandial blood pressure decline following a glucose drink on gait parameters in healthy older volunteers

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Aims The aims of this study were to determine if gait speed, stride length and double support percent time were affected by a blood pressure (BP) decline induced by the ingestion of a glucose (50g made up to 200 ml water) drink in healthy older volunteers.

Methods Four volunteers (mean age 73 years) have been recruited to date. Participants were studied on three randomised days (Day A, B, C). Day A involves ingestion of a glucose drink followed by ambulatory BP monitoring every six minutes for 60 minutes and then every 15 minutes until 120 minutes. Day B involves ingestion of 200ml water followed by ambulatory BP monitoring, as per Day A and gait analysis using the GAITRite walkway system every 30 minutes for 120 minutes. Day C involves ingestion of a glucose drink followed by ambulatory BP monitoring as per Day A and gait analysis as per Day B.

Results An average decline in systolic BP of 19 mmHg (mean) was seen following ingestion of the glucose drink (Day A). Walking every 30 minutes following the glucose drink (Day C) attenuated the fall in BP (mean decline in systolic blood pressure was 1.8mmHg) Compared to Day B, there appeared to be a reduction in measured gait parameters on Day C at 30 minutes.

Conclusions: Walking attenuates the fall in BP following ingestion of a glucose drink. The fall in BP following a glucose drink appears to impair gait parameters.

Intermittent walking: A potential treatment strategy for older people with postprandial hypotension

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Aim: The aim of this study was to determine the effects of intermittent walking on the systolic blood pressure (SBP) decline normally seen following ingestion of a 50g glucose drink in older people with postprandial hypotension (PPH).

Methods: Eleven volunteers were recruited. Participants were studied on two randomised days (control, intervention). Both days involved ingestion of a 50g glucose (in 200ml water) drink followed by ambulatory SBP and heart rate (HR) monitoring six minutely for 60 minutes, then 15 minutely until 120 minutes. On the intervention day, participants also walked at their usual pace for 30 metres every 30 minutes over 120 minutes following the drink.

Results: The median age was 75 years and 70% of subjects were female. Three participants had orthostatic hypotension and of these, two also had autonomic dysfunction. On the control day, a significant decline in SBP (P=0.009) was seen with the maximum fall of 20mmHg occurring at 60 minutes. On the intervention day, there was no fall in SBP (P=0.129). A statistically significant difference between the two days was noted in terms of the SBP area under the curve (Control: 1639 vs. Intervention: 601; P=0.016). There was no significant change in HR over time (Control: P=0.910; Intervention: P=0.790) on either day.

Conclusion: This study confirms for the first time that in older people with PPH, intermittent walking at a usual pace ameliorates the fall in SBP normally seen after a glucose drink. The lack of HR increase with PPH and exercise requires further investigation.

Is postprandial hypotension a possible contributing factor to hip fractures in older people?

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Background: The aetiology of falls in elderly are typically multifactorial and postprandial hypotension has been identified as one potential cause.

Objective: This study aimed to determine how commonly neck of femur fractures following a fall occurred within two hours of a meal and the factors independently associated with this circumstance.

Methodology: A prospective study was undertaken in the orthopedic unit at The Queen Elizabeth Hospital in South Australia. Consecutive first admissions of patients aged 70 years and over with a low impact neck of femur fracture between March and November 2011 were eligible. Patients or carers were interviewed using a standardised questionnaire within 72 hours.

Results: Data from 120 of 138 eligible patients were analysed. The median age was 84.0 years. Falls within two hours of a meal occurred in 21% patients. Among fractures occurring within two hours of a meal, there was a statistically significant difference in the percentage of fractures across the four time categories (P = 0.033) with the highest percentage (44%) of fractures occurring in the time category related to breakfast. Logistic regression analysis demonstrated that symptoms before the fall predicted falls occurring within two hours of a meal (OR 5.817; 95% CI 1.393 - 24.284).

Conclusion: PPH might be a contributing factor in up to 21% of hip fractures in older people. Patients with falls and symptoms of hypotension within 2 hours of a meal should be formally investigated for post-prandial hypotension to allow for intervention and prevention of falls.

Lay Description

A decline in blood pressure (BP) after a meal is common in the elderly. If this decline is excessive, this is termed post-prandial hypotension (PPH) and is associated with increased risk of falling and fractures. This study revealed that up to 21% of older patients admitted to hospital following a neck of femur fracture may have underlying PPH. Symptoms of low blood pressure following a meal may be an indicator of PPH, hence these patients should be investigated for post-prandial hypotension as they may be provided with simple treatment strategies that might prevent future falls.

The postprandial blood pressure decline following a glucose drink affects gait detrimentally in older people

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Background: Postprandial hypotension (PPH) is a risk factor for falls in older people. It is unknown if PPH is associated with changes in gait parameters.

Objective: To determine the impact of postprandial fall in systolic blood pressure (SBP) on gait speed, stride length and double support time in older subjects with and without PPH.

Methodology: SBP was measured in 24 older subjects 6 minutely for 60mins, then 15 minutely until 120mins following ingestion of a study drink on 3 randomised separate study days. On one day, subjects consumed 50g glucose in 200ml water and SBP was measured for a diagnosis of subjects with PPH. On the control (A) and intervention (B) days, subjects consumed water (A) or the same glucose drink (B) and gait speed was assessed at baseline then every 30mins for 120mins post drink ingestion.

Results: 13 subjects had PPH. In subjects with PPH, there was no change from baseline in SBP on A (P=0.830) or B (P=0.520). There was a significant decline in stride length on B (P=0.026) but not A (P=0.159). There was no change in gait speed (A: P=0.066; B: P=0.089) or double support time (A: P=0.066; B: P=0.089). In subjects without PPH, there was no change in gait speed (A: P=0.327; B: P=0.216) or stride length (A: P=0.110; B: P=0.153) on either study days. There was a significant change in double support time on A (P=0.032) but not B (P=0.506).

Conclusion: There was a significant reduction in stride length post oral glucose in older subjects with PPH; this may contribute to the increased falls risk in this group.

Lay Description:
Falls in older people usually have multiple causes. A decline in blood pressure after a meal, and changes in the way people walk or gait pattern, have been associated with increased falls risk. No studies have explored if there is a link between a post meal decline in blood pressure and a change in gait pattern. This study demonstrated that a decline in blood pressure after ingestion of a sugar drink is associated with a reduced walking stride length and this may contribute to an increased falls risk.

Appendix 4

Prizes recognising outstanding work

Australian & New Zealand Society for **Geriatric Medicine**

This is to certify that

Shailaja Nair

was awarded the

R M Gibson Prize

for the best presentation of a scientific paper by an Advanced Trainee

at the Australian and New Zealand Society for Geriatric Medicine
Annual Scientific Meeting, Adelaide, Australia 2013

Dated: 18th June 2013

President

THE QUEEN ELIZABETH HOSPITAL

Research Day 2013

This is to certify that

Shailaja Nair

has been presented with the prize
for Best Presentation in the category for:

Clinical Research Group 2

Dr Prue Cowled, Phd
Chairperson
TQEH Research Day 2013 Organising Committee

**Government
of South Australia**

SA Health

The Institute

basil hetzel institute for translational health research

**the hospital
research foundation**

finding cures improving care

THE QUEEN ELIZABETH HOSPITAL

Research Day 2014

This is to certify that

Shailaja Nair

has been presented with the prize
for Best Presentation in the category for:

Clinical Research Group 1

Dr Prue Cowled, PhD
Chairperson
TQEH Research Day 2014 Organising Committee

**Government
of South Australia**

SA Health

The Institute

basil hetzel institute for translational health research

**the hospital
research foundation**

finding cures improving care