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Volume 1

CHRONIC DISEASES IN GERIATRIC PATIENTS

Editor:
Tuck Yean Yong

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Volume 1

Chronic Diseases in Geriatric Patients

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PREFACE

A rise in prevalence of chronic non-communicable diseases, including heart disease, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, diabetes mellitus, stroke, cancers and osteoarthritis, have been observed among older people in many countries [1, 2]. A substantial and increased proportion of morbidity and mortality due to chronic disease occurs in older people. To compound this burden on the older individual and society in general, effective intervention is complicated by ageism, complex multiple comorbidity and lack of access to age-appropriate care. The purpose of this book is to address some of the medical care needs that exist for eleven common chronic conditions in older people. An additional chapter on end-of-life care will address the needs of older people with chronic diseases as they approach the terminal phase of life.

The chapter on coronary artery disease (CAD) in the elderly will look at the epidemiology, differences in clinical presentations and approach to evaluation and management that is appropriate for this age group. In particular issues on invasive assessment of the coronary artery and revascularisation procedures in older people with CAD will be addressed.

Heart failure is common in the older population and is associated with a poor prognosis. Managing older people with heart failure is a challenge because presenting features can be different from younger patients and the risk of adverse effects from polypharmacy. The chapter on heart failure aims to address these issues.

Hypertension is a common chronic condition in older people and an important risk factor for many vascular diseases. Therefore, the chapter on hypertension in older people will examine the evidence for controlling hypertension, target blood pressure and which antihypertensive agents to use in this age group.

Diabetes mellitus, especially type 2 diabetes, is a condition that affects many older people, about 20% of those aged ≥65 years. Like younger people, diabetes in the older age group is associated with significant morbidity, reduction in quality of life and mortality. In the older population, diabetes is associated with an increased risk of geriatric syndromes such as cognitive impairment, urinary incontinence and falls, which require careful assessment and management. The chapter on diabetes mellitus will look at some of the chronic problems faced by older people living with this condition.

Alzheimer's disease has emerged as a major public health concern globally which has a significant impact on the patient, family, caregivers and health care system. Although it has been recognised for more than a century, its pathogenesis is still not understood and benefits

from pharmacological treatment has been limited so far. The chapter on Alzheimer's disease will provide updates on neuroimaging, nonpharmacological and pharmacological treatment.

Ischaemic stroke is associated with one of the highest causes of disability in older people. Evidence suggest that older people with ischaemic stroke often receive less effective therapy and experience poorer outcomes compared with younger patients. The chapter on ischaemic stroke in this book will review the available evidence on secondary prevention and treatment of this condition in older people and reducing the disability burden among survivors after the acute event.

Many older people have chronic obstructive pulmonary disease (COPD) as a result of smoking and age-related pulmonary changes. COPD is associated with increased morbidity and mortality for the older population. The chapter on COPD will look at the diagnostic and therapeutic aspects of this condition that are relevant to the older age group.

Cancers are increasingly diagnosed among people aged ≥65 years and this age group makes up more than 50% of new diagnosis of malignancy. Cancer care in older people is complex and challenging which is further compounded by limited evidence on the risk-benefit of treatments. The chapter on cancers in the elderly will review the differences in approach to management and identify gaps in evidence related to care of this group of older patients.

Osteoarthritis, especially in the hip or knee, is a common diagnosis in older people that causes significant pain leading to disability and decreased quality of life. Management of osteoarthritis in these joints among the elderly is challenging because they often have multiple chronic conditions that can compound pain and increased susceptibility to adverse effects of analgesics. The chapter on osteoarthritis will review evidence-based nonpharmacological, pharmacological and surgical approaches to management of this condition in the hips and knees of older people.

Osteoporosis and fragility fractures are highly prevalent in older people, with the latter associated with significant disability, mortality and health care cost. Osteoporosis is still underdiagnosed and undertreated among older people. The chapter on osteoporosis will examine the efficacy of both nonpharmacological and pharmacological strategies in the management of this condition and prevention of associated fragility fractures among the older population.

The prevalence of chronic kidney disease (CKD) in the older population is steadily increasing worldwide. Management of CKD in older people is complex because there are many competing factors that have to be taken into consideration. One of the chapters will attempt to untangle some of these complexities and provide an updated review on a holistic approach in management of older people with CKD.

As most of the chronic diseases described in this book have no cure, it is inevitable that these diseases will affect older people at the end of life. Evidence indicates that technology-driven interventions at the end of life do not necessarily improve satisfaction with care or quality of life. As a result, the final chapter of this book will address the need for advanced care planning and provision of good quality end-of-life care that is in concordance with the older patients' and their family's or caregivers' goals.

In this book, the authors have sought to provide educational and updated reviews on common chronic diseases encountered in geriatric medicine. Although the chapters in this book are not an exhaustive list of all chronic diseases, they review conditions that are frequently managed as part of day-to-day clinical practice. Managing older people with chronic diseases require a holistic approach with comprehensive assessment, leading to well integrated continuing care and focusing foremost on patients' goals in an effort to streamline care.

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CHAPTER 1

Conundrums in the Care of Older Adults with Coronary Artery Disease

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Abstract: Coronary artery disease (CAD) is one of the leading causes of death in both men and women aged > 65 years. However, older patients have been underrepresented in clinical trials resulting in limited data about the effectiveness of different treatment strategies in this population. Furthermore, the atypical clinical presentations of CAD in elderly patients, often make diagnosis challenging and can lead to suboptimal implementation of treatment and secondary preventive measures by health care professionals. This chapter reviews clinical presentations and diagnosis consideration of CAD in the elderly. This review will also address clinical challenges that often arise when considering medication therapy and percutaneous coronary intervention (PCI) in the elderly, as well as cardiac rehabilitation in this population. To optimize the benefits of therapy in the elderly, providers should consider complex interplay of variables such as comorbidities, functional and socioeconomic status, side effects associated with multiple drug administration, and individual biological variability.

Keywords: Acute coronary syndrome, Angina, Bleeding risk, Coronary artery disease, Medication therapy, Older adults, Percutaneous coronary intervention, Polypharmacy, Revascularization.

OVERVIEW OF CORONARY ARTERY DISEASE IN THE ELDERLY

The clinical manifestations of coronary artery disease (CAD) in older patients represent the effects of the disease superimposed on the physiological

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Tuck Yean Yong (Ed)

effects of age. Mortality and morbidity from CAD is strongly associated with increasing age. The age–sex standardized mortality rate for age <75 years is 56 per 100,000 population, compared with 1437 per 100,000 population among those aged ≥75 years [1]. Amongst people aged ≥75 years, more than one third of men and approximately one quarter of women have been observed to have CAD [1]. As a consequence of population aging, it is estimated that the total elderly population will rise by 42% over the next decade [2 - 7]. As a result, older people will account for an increasing proportion of patients using healthcare services for treatment of symptomatic CAD. Autopsy studies show that more than one half of people older than 60 years of age have significant CAD, with high prevalence of left main or triple-vessel disease [3]. Coronary angiography studies also showed old patients have more extensive and complicated coronary artery disease, more frequent multivessel disease, more calcification of coronary artery, and are more likely to have had previous myocardial infarction (MI) [8, 9].

CLINICAL PRESENTATION OF CORONARY ARTERY DISEASE IN THE ELDERLY

Although CAD is prevalent in elderly persons, the disease is often not diagnosed or misdiagnosed in this age group. Failure to correctly diagnose the disease in the elderly may be due to differences in the clinical manifestation in this age group compared with younger patients. Such differences may reflect a difference in the disease process between older and younger patients or it may be related to the superimposition of normal aging changes. In addition, the presence of concomitant diseases may mask the usual clinical manifestations. An increased proportion of older patients compared to younger ones have atypical manifestations of myocardial ischemia, including dyspnoea and worsening heart failure [10]. Additionally, the frequent coexistence of chronic lung disease, gastroesophageal reflux disease, and other disorders may make CAD diagnosis more challenging. On the other hand, reductions in physical activity and aerobic exercise capacity may mask the symptoms in elderly CAD patients. The frequent coexistence of chronic lung disease, peripheral vascular disease, arthritis, and neurological disorders may make ambulation difficult. Therefore, a lack of exertional angina in an elderly patient with suspected CHD may merely reflect the patient's lack of significant activity. Clinical manifestation of acute coronary

syndrome (ACS) in the elderly may be more complicated [11]. Atypical presentations, absence of chest pain, dyspnoea, and symptoms related to comorbid diseases are common in elderly with ACS. Electrocardiographic changes are more often equivocal in the elderly, because of pre-existing bundle branch block or residual ST-elevation from previous infarct wall, and make electrocardiographic interpretation challenging. Cardiac troponin elevation can be seen in conditions other than ST-segment elevation myocardial infarction (STEMI), and many of these conditions such as heart failure, pulmonary embolism, sepsis, end-stage kidney disease, stroke, and so on are increasingly prevalent with age [12].

DIAGNOSTIC CONSIDERATION OF CAD IN THE ELDERLY

The evaluation of an older person with suspected CAD should begin with a detailed history and full physical examination, and ascertainment of the coronary risk factors and comorbid illnesses. After initial assessment of clinical stability, it is necessary to stratify patients to high- or low-risk group. Clinical outcomes in elderly patients with CAD are directly related to left ventricular function, the extent of vascular disease, and the presence of comorbidities [9, 10]. So assessment of heart function and coronary artery lesion severity by noninvasive or invasive imaging tests are also important. Additionally, stress testing is critical in stratifying older patients with myocardial ischemia, especially those who are asymptomatic.

SPECIAL CONSIDERATIONS FOR MEDICAL THERAPY IN ELDERLY PATIENTS WITH CAD

The principal goals in the care of patients with CAD, are to establish the diagnosis, relieve symptoms, and to prevent future cardiac events such as ACS, revascularization, or death. Pharmacological therapy plays an important role in achieving these goals. Beta (β)-blockers are preferred for initial treatment of symptoms. Calcium channel blockers and nitrates can be used to provide symptom relief when initial treatment with β-blockers is ineffective, contraindicated or causing side effects. Ranolazine, a piperazine derivative, produces its antianginal effects without decreasing heart rate or blood pressure. Ranolazine has been used effective in improving angina symptom in patients who

CHAPTER 2

Treating the "Young at Heart": Management of Heart Failure in the Older Population

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Abstract: The prevalence of heart failure rises with increasing age. Although patients with heart failure are mainly elderly (age ≥65 years), evidence for efficacious diagnostic and therapeutic approaches are limited in this population. Diagnosis of heart failure in older people is challenging because of comorbidities masking symptoms and signs; different diagnostic cut-offs of natriuretic peptides; and the high prevalence of heart failure with preserved ejection fraction (HFPEF). Geriatric syndromes (such as cognitive impairment, frailty, falls and incontinence) are common in heart failure and can affect patients' prognosis. In older patients with reduced ejection fraction, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and beta-blockers have improved clinical outcomes. However no therapeutic strategy has yet been found to improve prognosis of HFPEF which affect many older people.

Keywords: Ageing, Cardiac devices, Diagnosis, Ejection fraction, Elderly, Geriatric syndromes, Heart failure, Left ventricular function, Systolic dysfunction, Therapy.

INTRODUCTION

Heart failure is largely a disorder of the older people and as the population ages; its prevalence is expected to rise to epidemic proportion [1]. People aged 65 years

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and older account for more than 75% of hospitalizations related to heart failure [2]. In the US each year, nearly ten new cases of heart failure are diagnosed in every 1000 people aged over 65 years [3]. The American College of Cardiology and American Heart Association defines heart failure as "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood" [3].

Although heart failure occurs more frequently in older people, current diagnostic and therapeutic recommendations are derived largely from studies that have included few people in this age group. The purpose of this chapter is to review the diagnosis of heart failure in older people and effectiveness of different management strategies including non-pharmacological, pharmacological, common associated geriatric syndromes and device-related therapies in this age group.

CLINICAL FEATURES

Fatigue or dyspnoea on exertion, with or without some degree of peripheral oedema, are the more common early symptoms of heart failure in older people [4]. With progression of heart failure, especially if untreated, dyspnea on exertion eventually occurs even at rest or fatigue becomes more severe. Such symptom may not always be apparent in older people because of restricted physical activities, therefore delaying diagnosis. Orthopnoea and paroxysmal nocturnal dyspnea are more specific symptoms for heart failure in older people [4, 5]. Oedema associated with heart failure is always symmetrical and pitting. It generally begins with foot and ankle, extends proximally and can involve the scrotal area, sacral region and abdomen. Chronic severe oedema can lead to skin changes such as brown pigmentation, induration and skin blisters. Other less frequent and atypical symptoms of heart failure in older people include syncope, angina, nocturia, oliguria and changes in mental status.

In the physical examination of an older person with heart failure, an elevated jugular venous pressure is the most specific sign of fluid overload [6]. Other physical signs such as pulmonary crackles, third heart sound or leg oedema may not always be present in chronic heart failure and may be caused by other

conditions [7].

EVALUATION OF HEART FAILURE IN OLDER PATIENTS

Heart failure has to be evaluated as a syndrome and not a disease. It often has an identifiable underlying cause. Coronary artery disease and hypertension are two of the more common causes of heart failure across all age groups, including older people [8, 9].

The most clinically relevant classification of heart failure into systolic dysfunction or preserved systolic function is based on left ventricular ejection fraction, which is most commonly assessed by transthoracic echocardiography. Determining if the systolic function is preserved or not has both prognostic and therapeutic implications [10]. Heart failure with reduced left ventricular ejection fraction is defined as clinical heart failure with left ventricular ejection fraction <45% [11]. Systolic heart failure is characterized by an enlarged and weakened left ventricle that is impaired in producing a normal stroke volume and cardiac output. Epidemiological data suggest that about 50% of all heart failure patients have a preserved ejection fraction, also known as diastolic heart failure [12]. Heart failure with preserved left ventricular ejection fraction (HFPEF) is defined as clinical heart failure with normal or near normal left ventricular ejection fraction, generally 55% or greater [13]. To make a clinical diagnosis of HFPEF, determination of diastolic dysfunction is not essential but abnormalities in active and passive relaxation are commonly observed [14]. Over half of all heart failure in the older population have normal left ventricular ejection fraction [15].

Measuring plasma levels of brain natriuretic peptide (BNP) is useful for the triage of patients with suspected heart failure [16]. BNP improves the diagnostic evaluation of heart failure in older people when added to assessment of symptoms and signs [17]. However there are a few limitations to the use of BNP in older patients such as increase in levels related to advancing age, renal impairment and chronic obstructive pulmonary disease [18, 19]. In people aged >70 years, change of N-terminal-pro-Brain-Natriuretic Peptide (NT-proBNP) over time, correlates independently with all-cause and cardiovascular mortality [20].

CHAPTER 3

Updates on Treating Hypertension in Older People

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Abstract: Our population is ageing, and as older people (≥65 years of age) are affected by hypertension, these individuals are at increased risk of organ damage or cardiovascular disease (CVD). They pose many management dilemmas because most hypertension trials had upper age limits with participant recruitment or did not present age-specific results. Because evidence-based guidelines have limited information on managing older patients with hypertension, recommendations are mostly based on expert opinion. Drug treatment for elderly hypertensive patients are generally recommended but with a greater degree of caution because of changes in drug distribution and elimination, as well as the need to consider quality of life factors. However, patients in most hypertension trials were aged <80 years. Pooling the limited number of octogenarians from several trials, this group of treated patients showed a reduction in both stroke and cardiovascular (CV) morbidity, but a trend toward higher all-cause mortality compared to controls.

Therefore, the overall benefits of lowering the blood pressure in octogenarians remain unclear despite epidemiological evidence that hypertension remains a major CV risk factor in this age group. Resistant hypertension (*i.e.*, blood pressure that remains above target when patient adheres to lifestyle measures and maximum tolerated doses of complementary antihypertensive agents which usually includes a diuretic) is more frequent with advancing age. Older patients with higher baseline systolic blood pressure characteristically have more severe or longer duration of hypertension, resulting in more difficult blood pressure control because it is often associated with autonomic dysfunction and organ damage.

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Keywords: Angiotensin-converting enzyme inhibitors, Antihypertensives, Beta-blockers, Calcium channel antagonists, Cardiovascular diseases, Denervation of renal artery, Diuretic, Elderly, Hypertension.

INTRODUCTION

Hypertension is defined as a systolic blood pressure (SBP) of ≥140 mmHg or diastolic blood pressure (DBP) of ≥90 mmHg. Isolated hypertension is a SBP of ≥140 mmHg with a DBP of <90 mmHg [1]. Stage 1 hypertension is SBP of 140-159 mmHg with DBP of 90-99 mmHg while stage 2 is SBP of ≥160 mmHg or DBP of ≥100 mmHg [1]. Prehypertension is defined as SBP of 120-139 mmHg with DBP of 80-89 mmHg [1]. Resistant hypertension is defined as resistance to lower SBP and DBP values below 140 and 90 mm Hg, respectively, despite the use of three optimally dosed antihypertensive drugs from different classes with one of the medications being a diuretic [2].

The prevalence increases significantly with age, such that about two-thirds of those aged >60 years have hypertension [3]. Hypertension is a major risk factor for cardiovascular (CV) disease in older people. Hypertension is present in 69% of patients with a first myocardial infarct [4], 77% of those with a first stroke [4], 74% of those with heart failure [4] and 60% of those with peripheral vascular disease [5].

PATHOPHYSIOLOGY

Most cases of hypertension are caused by reduced elasticity and compliance of large arteries arising from ageing and from the atherosclerosis-associated accumulation of arterial calcium and collagen as well as arterial elastin degradation. Loss of arterial elasticity causes an elevation in the rate of return of reflected arterial pressure waves from the periphery, hence increasing the peak systolic pressure [6]. Rise in blood pressure (BP) itself can lead to further arterial stiffening and impairment in endothelium-dependent vasodilatation [7, 8].

EVALUATION

Assessment of an older person with hypertension should include evaluation for the presence of other CV risk factors, potentially contributing lifestyle factors,

end-organ damage, and concomitant diseases affecting prognosis and treatment [9]. Physical examination must include evaluation of optic fundi, thyroid, heart, lungs, kidneys, peripheral pulses and the neurological systems. In rare situations, peripheral arteries can become so rigid that measuring BP with the standard arm cuff may lead to overestimating arterial pressure because of incomplete compression of the brachial artery [10]. Pseudohypertension should be considered when patients' blood pressure do not respond to therapy as expected or who have postural symptoms with treatment.

Laboratory tests and electrocardiography should be performed to evaluate CV risk and end-organ damage. Laboratory tests should include urinalysis, blood glucose, serum potassium, estimated glomerular filtration rate and lipid profile. Evidence of target organ damage will support a diagnosis of suboptimally-controlled BP and may affect decisions about appropriate treatment selection.

In patients with persistent office hypertension but no end-organ damage, ambulatory BP monitoring is recommended to determine if white-coat hypertension is contributory. Ambulatory BP monitoring is indicated when the diagnosis of hypertension or response to therapy is unclear from office visits, when syncope or hypotensive disorders are suspected, and symptoms of vertigo or dizziness require evaluation.

BLOOD PRESSURE GOALS IN OLDER PEOPLE

The American Academy of Neurology, the American Geriatrics Society, the American Society of Preventive Cardiology, the American Society of Hypertension, the American Society of Nephrology, the Association of Black Cardiologists and the European Society of Hypertension, the American College of Cardiology Foundation and American Heart Association (ACCF/AHA) 2011 expert consensus on hypertension in the elderly recommended that the SBP be reduced to <140 mmHg in older persons of less than 80 years and to 140-145 mmHg if tolerated in those aged 80 years or older [1]. These guidelines were based on data from the Systolic Hypertension in Elderly Program (SHEP) [11 - 13] and Hypertension in the Very Elderly (HYVET) [14] trials.

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CHAPTER 4

Crossing New Frontiers in the Care of Older Adults with Diabetes Mellitus

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Abstract: Diabetes mellitus has a significant impact on the health and well-being of older people with this condition. The prevalence of diabetes and its associated complications is increasing in older people, leading to decline in functional status and quality of life. The appropriateness of tight glycaemic, blood pressure and lipid control for an older person with diabetes needs to be assessed individually. Although many pharmacological treatments for diabetes are available, their use in older people can be challenging due to increased risk of adverse reactions and drug-drug interactions with other medications. Rates of geriatric syndromes (*e.g.* depression, cognitive impairment, functional disability, urinary incontinence and falls) are increased in older people with diabetes. Multidisciplinary and multidimensional approach to management is essential to maintain independence and quality of life in older people with diabetes.

Keywords: Cardiovascular diseases, Diabetes mellitus, Geriatric syndromes, Glycated haemoglobin, Hyperglycaemia, Hypertension, Hypoglycaemia, Individualized therapy, Older people.

INTRODUCTION

Diabetes mellitus is more common in the older population. More than 20% of the US population aged ≥65 years has diabetes [1] and the ageing population is a

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significant driver of the diabetes epidemic. Similarly in China, the prevalence of diabetes in the population aged 60 years and above was about 20% [2]. Older people with diabetes may either have newly diagnosed disease (diagnosed after 65 years of age) or long-standing diagnosis with onset before 65 years of age. Older people with diabetes have type 2 diabetes (>90%) and 75% of them are estimated to require insulin therapy [3]. The burden of diabetes in older people is associated with higher mortality, reduced functional status and increased risk of institutionalization [4]. Older adults with diabetes are also at higher risk for both acute and chronic cardiovascular and microvascular complications related to this disease.

The treatment of diabetes in the older population, especially the older old (aged ≥80 years), is often challenging because therapy options are limited by their physical, psychological and cognitive functions. Older patients with diabetes may have increased risk for frailty and functional dependency [5]. Although there is currently no gold standard definition of frailty, it is generally considered to be a multi-factorial condition characterised by a heightened vulnerability to changes in health status [6]. This chapter will focus on the features of diabetes relevant to older people, currently available treatment options, geriatric syndromes in the setting of diabetes and challenges of management in this age group.

PATHOGENESIS

Older people are at higher risk for developing type 2 diabetes because insulin resistance increases and pancreatic islet function declines with increasing age. Age-related insulin resistance has been found to be associated with adiposity, sarcopenia and physical inactivity [7]. In addition, age-related deterioration in pancreatic islet function and islet proliferation have also been reported [8 - 10].

Insulin secretion has been observed to decline with age, with considerably diminished β-cell sensitivity and acute insulin response [11]. In contrast to younger people, insulin resistance in older people with type 2 diabetes seems to predominate in skeletal muscle, whereas hepatic glucose output is almost unaffected [11]. One of the most striking changes in older people with type 2 diabetes is the presence of insulin resistance in the absence of obesity, which

could be linked to mitochondrial dysfunction in skeletal muscle and increased fat accumulation in muscle and liver tissue [12, 13]. Type 2 diabetes in older lean people is usually associated with a significant impairment in glucose-induced insulin secretion, whereas in older obese people, the main deficit seems to be resistance to insulin-mediated glucose disposal [13, 14].

SCREENING AND DIAGNOSIS

Clinical presentation of diabetes in old age is often non-specific and asymptomatic resulting in delay in diagnosis. In general, screening and diagnosis of diabetes in older subjects should be in accordance with published international or national criteria and guidelines [15, 16]. Currently no age-defined criteria has been proposed. Frequent healthcare contact for other medical problems in the absence of diabetes-related symptoms may reveal incidental cases of diabetes. For example type 2 diabetes in older people can present as falls, urinary incontinence and changes in cognition or behaviour.

Three important factors have been identified that increase the value of screening for diabetes: age ≥55 years, systolic blood pressure of ≥130 mmHg, or a body mass index ≥35 kg/m^2 [17]. However no agreement exists on the best screening test for diabetes in people aged ≥55 years. When fasting plasma glucose is the only criterion used, the prevalence and incidence rates of diabetes in older people (>65 years) may be underestimated [18]. In higher-risk older people with a normal fasting glucose where an oral glucose tolerance test (OGTT) is not feasible, determination of glycated haemoglobin (HbA_{1c}) may be helpful in the diagnosis of diabetes [19]. An HbA_{1c} 48 mmol/mol or >6.5% may indicate the likely presence of diabetes [19].

ASSESSMENT

Older patients with type 2 diabetes should have an evaluation of their overall functional status using well-validated assessment tools [20]. Incorporating a comprehensive geriatric assessment will ensure the assessment of three major domains: global/physical, cognitive and affective [20]. In older adults with diabetes, functional status can dictate the screening, preventive, diagnostic and therapeutic approach, including therapeutic targets.

CHAPTER 5

Halting the Decline in Cognition: New Insights into Alzheimer's Disease

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Abstract: Alzheimer's disease is a major public health concern globally and has been identified as a research priority. Although this disease has been recognized for more than a century, there is an urgent need to improve our understanding of its pathogenesis in order to advance development of disease-modifying treatments. Clinical diagnosis of Alzheimer's disease remains the main method of identifying the disease but neuroimaging and biomarkers are emerging as adjunct tests in selective cases. Only a few pharmacological treatments are available for Alzheimer's disease and modest benefits are only observed in the mild-to-moderate disease. Without effective treatment, non-pharmacological approaches and prevention remain important. Non-pharmacological approaches such as exercise, cognitive stimulation therapy and computerized mind games are potentially beneficial in slowing the progression of Alzheimer's disease. Behavioural and psychological symptoms in Alzheimer's disease are still challenging to manage and require a combination of non-pharmacological and pharmacological approaches. Several novel therapies are currently under investigation and clinical trials of these agents will reveal if they are beneficial in the treatment of Alzheimer's disease.

Keywords: Alzheimer's disease, Anticholinesterase inhibitors, Behavioural symptoms, Carers, Cognitive impairment, Dementia, Diagnosis, Lifestyle modifications, Memantine, Psychological symptoms, Treatment.

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INTRODUCTION

Alzheimer's disease is the most frequent cause of dementia in many countries. It was first named by Alois Alzheimer more than a century ago after examining a 51 year-old woman who was disoriented in time and place. He observed that "her ability to retain information is impaired to the profoundest degree" [1]. Interestingly in 2013, this patient's disease was finally understood when her DNA was found to have a rare mutation in the presenilin 1 gene that causes early onset Alzheimer's disease [2].

Alzheimer's disease has a significant impact on those with the condition as well as family and caregivers. Progression of the disease leads to loss of functional independence, the need for residential care and medical complications resulting in deaths.

EPIDEMIOLOGY

The Delphi study estimated that there were about 24 million people worldwide with dementia in 2001 and the majority are thought to have Alzheimer's disease [3]. It is predicted that the figure will rise to 42.3 million in 2020 and 81.1 million by 2040.

In 2010, 35.6 million people were estimated to have lived with dementia worldwide, with numbers predicted to increase two-fold every 20 years, to 65.7 million in 2030 and 115.4 million in 2050 [4]. In 2010, 58% of all people with dementia lived in countries with low or middle incomes, with this proportion anticipated to rise to 63% in 2030 and 71% in 2050.

RISK FACTORS

A consensus report from a panel of experts summarized some of the most consistently identified risk factors in Alzheimer's disease [5]. They found that smoking, depression, diabetes mellitus, metabolic syndrome and the apolipoprotein e4 (APOE e4) gene mutation were associated with increased risk of cognitive decline. The most prevalent genetic risk factor for late onset disease is the apolipoprotein ε4 allele, a gene for lipid transport in the brain. Over 65% of people with Alzheimer's disease are carriers of ε4 but only about 15% of the

population possess it [6].

A family history of dementia is one of the most consistently reported risk factors for Alzheimer's disease [7]. Among patients with late-onset disease, first-degree relatives have about a two-fold increase in their lifetime risk of the disease [7]. In addition, the disease is more concordant in monozygotic twins than dizygotic twins [8]. Apart from genetic factors, many treatable medical conditions are also associated with an increased risk of Alzheimer's disease, including stroke, hypertension and hypercholesterolaemia [9 - 11].

PATHOGENESIS

There are three main hypotheses on the pathogenesis and aetiology of Alzheimer's disease: the amyloid plaques, neurofibrillary tangles and changes in neurotransmitter levels such as acetylcholine.

The amyloid hypothesis proposes that the pathological formation of amyloid plaques are directly toxic to cells and disrupt neurotransmission. These extracellular plaques are mainly made up of insoluble fibrils of amyloid beta (Aβ) peptide, which is formed when β-secretase and γ-secretase enzymes cleave amyloid precursor protein (APP). The ε4 allele is thought to promote deposition of Aβ [6]. However Aβ deposition does not correlate strongly with brain atrophy; nor is it detected consistently in people with early Alzheimer's-like neurodegeneration [12].

"Hyperphosphorylated" tau has been hypothesized as the cause of neurofibrillary tangles [13]. Tau, an insoluble protein, stabilises microtubules which in turn maintain the axons connecting neurons to one another. Hyperphosphorylated tau is thought to weaken axons because it does not bind to microtubules and it also forms protein filaments, which lead to neurofibrillary tangles. Neurofibrillary tangles correlate better with cognitive status and neuronal loss than the presence of amyloid plaques [14].

The third hypothesis focuses on the neurotransmitter acetylcholine. In people with Alzheimer's disease, less acetylcholine is present in their brains compared to those without dementia [15]. It is postulated that degeneration of the basal

CHAPTER 6

New Horizons in Ischaemic Stroke among Older People

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Abstract: The incidence and prevalence of ischaemic stroke increase substantially with age. In addition, clinical outcomes after a stroke are influenced significantly by age. Risk factor profiles for ischaemic stroke differ between young and older patients. Furthermore older patients with ischaemic stroke often receive less effective treatment and experience poorer outcomes than the younger population. For those who survive an acute ischaemic stroke, a comprehensive approach involving lifestyle modifications, antiplatelet or anticoagulant therapy, blood-pressure control, cholesterol-lowering and carotid artery stenosis intervention where applicable, is effective in reducing the risk of recurrent stroke. Long-term rehabilitation and supportive care is critical in the management of older people after an acute ischaemic stroke. Future research is still needed to reduce the incidence of ischaemic stroke and improve outcomes in the older population..

Keywords: Anticoagulant, Antiplatelet therapy, Carotid artery stenosis, Hypertension, Older, Rehabilitation, Risk factors, Secondary prevention, Stroke.

INTRODUCTION

Worldwide, about 16 million first episode of stroke occur annually and 5.7 million die from it each year [1]. Stroke is the second most common cause of death after

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myocardial infarction [1] and is associated with one of the highest rates of disability in adults [2]. Up to 50% of stroke survivors were unable to regain independence and need long-term personal care [3]. Stroke can affect individual of any age but the incidence and prevalence increase significantly with advancing age [4]. For each successive decade after the age of 55 years, the rate of stroke doubles in both men and women [5]. With an aging population, the incidence and economic burden of ischaemic stroke is expected to rise.

Patients with stroke are at increased risk for further vascular events including recurrent ischaemic stroke (highest risk), acute myocardial infarction and death from other vascular causes. The risk of recurrent stroke is highest in the early period after an acute event and therefore, secondary prevention strategies are essential [6]. Older people who survive an acute ischaemic stroke often need long-term rehabilitation and supportive care.

This chapter will examine the differences in clinical outcomes among older people who experience ischaemic stroke in comparison to the younger population and review secondary prevention strategies and rehabilitation approaches after a stroke event.

CLINICAL OUTCOMES AND EVALUATION

In comparison to younger patients, older people with strokes have more severe neurological deficits at presentation and they recover more slowly [7, 8]. Older people who survive a stroke are more likely to require assistance in activities of daily living or to need care in a residential facility compared to younger patients [9]. This difference can be explained by medical and functional status before the stroke, pre-existing multiple organ dysfunction, polypharmacy and severity of stroke [7, 10].

After the first ischaemic stroke or transient ischaemic attack (TIA), people aged >65 years have a three-fold increase in risk for a recurrence within the next 10 years compared with those below this age [11]. Increasing age has been observed to be an independent risk factor associated with mortality both in the short- and long-term after acute ischaemic stroke [12]. In several studies, the stroke mortality rate is highest among people aged 75 years and above but the reason is uncertain

[12, 13]. Several important factors may be contributory including stroke severity, higher frequency of atrial fibrillation (which is associated with higher mortality) [14] and the presence of comorbidities [10].

In the evaluation of stroke or TIA, brain imaging is mandatory for diagnosis, classification and management. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) in the diagnosis of acute ischaemic stroke [15] but it may not be available widely. Next, arterial imaging with the use of carotid Doppler ultrasonography, CT angiography or magnetic resonance angiography (MRA) is usually necessary. Electrocardiography (ECG) must be performed to identify if atrial fibrillation is present. Occasionally ambulatory ECG is needed to detect paroxysmal atrial fibrillation. Transthoracic or transoesophageal echocardiography is often used to identify cardiac sources of embolism other than atrial fibrillation. Blood investigations are useful to show other contributing factors such as primary erythrocytosis, hyperglycaemia, kidney dysfunction and electrolyte disturbances.

STROKE UNITS

Admission to a stroke unit has been demonstrated to benefit patients of all ages [16, 17]. Such care may enable an extra five patients out of every 100 to return home [18]. Early mobilisation and correction of abnormal physiological parameters after stroke have been shown to improve stroke care, minimize disability and complications, improve long-term survival and decrease the risk of recurrence [15, 19, 20].

SECONDARY PREVENTION

Intensive risk factor treatment and lifestyle modification are essential in all patients after an acute ischaemic stroke, regardless of age. It is estimated that at least 80% of recurrent events might be prevented with the use of a comprehensive approach that includes exercise, dietary modification, antiplatelet or anticoagulant therapy, blood pressure and cholesterol control [21]. Carotid endarectomy should be considered in selective patients [22]. Observational studies of patients with a previous stroke showed that healthy lifestyle behaviours including regular exercise and abstinence from smoking are associated with a reduced risk of

CHAPTER 7

Chronic Obstructive Pulmonary Disease in Older People: Breathing Deeper with Age

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Abstract: Chronic obstructive pulmonary disease (COPD) is one of the most common chronic diseases in older people. COPD in the older population is a challenging disorder to diagnose and manage because of several unique age-related aspects. Age-related changes in pulmonary function can predispose older people to increased risk of mortality and other complications from COPD. The established Global Initiative for Obstructive Lung Disease criteria can be applied effectively to older people with COPD. This approach requires the use of spirometry which can be performed satisfactorily in most older patients. Treatments that are effective to reduce acute respiratory exacerbations include smoking cessation, vaccinations against influenza and pneumococcus, and the use of short- and long-acting bronchodilators. Other beneficial management strategies for COPD in older adults include pulmonary rehabilitation, domiciliary oxygen and noninvasive positive airway pressure when indicated. Care should also be focused on common comorbidities associated with COPD as these can often complicate the health of older people.

Keywords: Bronchodilators, Chronic obstructive pulmonary disease, Comorbidities, Corticosteroids, Diagnosis, Domiciliary oxygen, Management, Older, Palliative care, Pulmonary rehabilitation, Smoking cessation, Spirometry.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common chronic disease in

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older people, affecting about 14% of those aged 65 years and above [1]. It is responsible for about 20% of hospital admissions of people aged 65 to 75 years [2]. COPD is associated with significant morbidity and ranks as the fourth leading cause of death worldwide. Although the burden of COPD is increasing in older people, underdiagnosis and undertreatment in this age group remain a frequent problem [3].

This chapter will focus on the diagnosis, management and prevention of COPD particularly aspects that are relevant to older adults. It will also look at the need to manage common comorbidities that are present in older patients with COPD.

AGE-RELATED CHANGES IN RESPIRATORY SYSTEM

Peak pulmonary function is usually approached at about the age of 20 years. After that, airflow limitation increases with age because of decline in lung elastic recoil, chest wall stiffness and respiratory muscle weakness [4]. Lung elastic recoil is influenced by collagen and elastin. Loss of elastic recoil with age is related to increased cross-linking of collagen and degeneration of elastin [5]. Furthermore bronchiolar airway size generally decreases after the age of 40 years irrespective of lung disease [5]. Other lung changes with increasing age include larger diameter of the alveolar ducts, smaller alveolar sacs and increase in alveolar basal laminae [5]. The overall changes of this airway pattern will lead to "senile emphysema" which can occur in non-smokers and still resemble smoking-related COPD. These age-related changes are different from airflow limitation caused by COPD, which is largely a consequence of parenchymal destruction and small airway disease.

COPD is characterised by the progressive airflow limitation, worsening slowly over years. The forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) declines with age. On the other hand, residual volume (RV) increases with age. However there is no correlation between age and total lung capacity (TLC).

Ageing also lead to reduced chest wall compliance [4]. The loss of chest wall compliance can be a result of kyphoscoliosis, calcification of intercostal cartilage and arthritis of costovertebral joints. Moreover there are decreases in lateral

intercostal muscle and diaphragm strength in older people compared to younger ones [4].

Of concern, older people have decreased perception of increases in airway resistance and less peripheral sensitivity to carbon dioxide [4]. The latter can lead to an impaired ventilatory response if hypercapnia occurs. These changes may result in disconnection between symptoms experienced and severity of respiratory dysfunction as well as delays in seeking medical attention.

EVALUATION

Clinical features commonly associated with COPD include chronic cough, persistent sputum production, dyspnoea and risk factors such as smoking and occupation-related exposure to inhaled toxins. However clinical assessment alone in older people with COPD can be challenging.

Spirometry is an objective and essential diagnostic tool of COPD and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines use spirometry measurements to determine disease severity (Table **1**) [6]. Based on these guidelines, COPD is diagnosed in the presence of FEV_1/FVC of <0.7. In one study of community-dwelling older people, 75-80% was able to perform valid spirometry [7]. However frail older adults with cognitive impairment may have difficulties performing spirometry. Spirometry should be performed only in symptomatic individuals followed by postbronchodilator measurement if airflow obstruction is detected. In older people, the GOLD spirometry criteria may lead to overdiagnosis of COPD because of the lung changes that occur normally with age, as described earlier. Up to 20% of older people may be incorrectly diagnosed with COPD if spirometry criteria alone are used without consideration of clinical manifestations [8].

Other pulmonary testing may also be useful for COPD diagnosis. Lung volumes are also related to symptom manifestation and functional limitation in COPD. Hyperinflation, measured as lung volume measurements of inspiratory capacity/total lung capacity, predicts survival better than FEV_1 in COPD [9]. A reduction in the diffusion capacity of carbon monoxide is another useful clue to the presence of COPD. A 6-min walk test is also useful to determine whether

CHAPTER 8

Cancer in Older Adults: To Treat or Not to Treat?

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Abstract: The incidence of cancer in older people (aged ≥65 years) is about 8-fold higher than in the younger population and there is a growing number of cancer survivors living beyond the age of 65 years. When cancer is suspected or diagnosed in an older person, clinicians face many challenges related to diagnosis and management. Treatment decisions in older cancer patients need to take into account the individual's level of function and reserve. The best approach to assess an older individual's medical, psychological and functional capabilities is through the application of a Comprehensive Geriatric Assessment (CGA). CGA has been shown to predict treatment outcomes and survival in oncology settings as well as guide the implementation of multidisciplinary interventions. The goals of cancer treatment in older adults should be cure if possible and prolongation of active life expectancy as well as maintaining quality of life. There is still a dearth of clinical trials evaluating cancer treatment in the older people; an issue which needs to be addressed urgently as the population ages.

Keywords: Cancer, Chemotherapy, Diagnosis, Frailty, Geriatric, Malignancy, Multidisciplinary, Older, Oncology, Quality of life, Survivorship, Treatment.

INTRODUCTION

The incidence of many cancers increases with age [1]. As a result of population ageing, cancers are increasingly diagnosed. In many countries, more than 50% of

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newly diagnosed cancers occur among people aged ≥65 years [2].

Cancer is a major cause of mortality worldwide, accounting for an estimated 9.9 million yearly, of which 54% occur in people aged ≥60 years [1]. As early detection and treatment options have expanded, long-term cancer survival has improved and the number of survivors living in their older age is growing [3].

Cancer care in the older people is complex and challenging. When cancer is suspected or diagnosed in older people, multiple challenges arise including diagnostic and treatment uncertainties because of limited evidence on risk-benefit [4]. In addition, providing comprehensive survivorship care to older people can be challenging.

The purpose of this chapter is to review the clinical differences in older cancer patients, approach to their management, provision of survivorship care and gaps in evidence related to their care.

CANCER IN DIFFERENT AGE GROUPS

In contrast to younger people, the presentations of cancers among elderly are often non-specific and may be obscured by other co-existing conditions which can lead to underdiagnosis and diagnosis at a more advanced stage [5]. In older people, multiple malignancies are common at presentation, occurring in up to 20% [6]. Another difference for older people with cancer is the higher frequency of functional disability; 20% have impaired activities of daily living (ADL) and 70% have impaired instrumental activities of daily living (IADL) [7, 8]. The state of increased frailty reduces the benefits of cancer treatment and increases their vulnerability to therapy-related complications [9].

Ageing is characterised by decreased homeostatic reserve which can affect cardiovascular, renal, immunological and haematological systems which are relevant to cancer treatment [10]. In addition, age-related changes in drug pharmacokinetics, pharmacodynamics and metabolism need to be taken into account in treating older people with cancer. Other important differences to take into consideration include polypharmacy, social isolation and more competing concurrent diseases which are more common in the older adults [11, 12]. Geriatric syndromes such as cognitive impairment, delirium, malnutrition and falls can

affect cancer therapy or arise as complications of treatment [13].

The older population is heterogenous and functional reserve of organ systems are poorly reflected by chronological age. As a result there is great variability in health and functional status among older adults of the same chronological age. In contrast, physiological age is more important in decision-making for cancer treatment.

ASSESSMENT OF OLDER PEOPLE WITH CANCER

Comprehensive geriatric assessment (CGA) is one of the most useful ways of estimating one's physiological age in cancer care (Table **1**). CGA is a multidimensional process focused on evaluating an older person's medical, psychological and functional status to facilitate integrated planning of treatment [14]. In a meta-analysis of 28 controlled trials, the use of CGA was associated with reduced risk of mortality, reduced hospital readmissions, improved physical function and increased likelihood of living at home [15]. In oncology clinical trials, CGA was useful in identifying unsuspected geriatric problems and syndromes [16 - 18], predicting treatment outcome and survival [19 - 22] and developing multidisciplinary interventions [23, 24].

Table 1. Comprehensive Geriatric Assessment domains and potential clinical applications.

Domain	Clinical Application
Functional status Activities of daily living Instrumental activities of daily living	Estimate life expectancy Determine functional independence
Comorbidity Comorbidity indices	Estimate life expectancy
Cognition Mini-mental State Examination	Determine life expectancy and functional independence
Mood Geriatric Depression Scale	Indicate motivation to engage in treatment
Nutrition Mini Nutritional Assessment	Potentially reversible condition
Polypharmacy	Risk of drug interactions

CHAPTER 9

Overcoming Osteoarthritis in Old Age

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Abstract: Osteoarthritis is a common diagnosis in older people aged 65 years and above, which causes significant pain leading to disability and decreased quality of life. Nonpharmacological measures such as exercise and footwear are essential in the management of osteoarthritis-related pain and disability in the older population if medication adverse effects and polypharmacy are to be avoided. Pharmacological approaches to pain management should complement nonpharmacological treatment. Most drug therapies give mild-to-moderate pain relief but their long-term efficacy and safety in older people remain undetermined. In older patients with severe osteoarthritis of the hips or knees responding poorly to analgesics, total joint arthroplasty offers the most effective intervention for those who are fit for surgery.

Keywords: Analgesia, Arthroplasty, Elderly, Exercise, Footwear, Knee, Hip, Osteoarthritis, Pain management, Physical therapy, Surgery.

INTRODUCTION

Osteoarthritis is one of the leading chronic condition causing functional decline and morbidity in older people aged ≥65 years [1]. Osteoarthritis involving joints in the lower limbs is a leading cause of impaired mobility and disability in older people [2]. The prevalence of osteoarthritis increases with age and with an ageing population, this condition will have a significant burden on health care [3]. Management of osteoarthritis-related pain is a challenge in older people. In this age group, undertreatment of pain can lead to decreased mobility, cognition and

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self-related health, which can threaten independence [4, 5]. Older people often have multiple chronic conditions that can compound osteoarthritis-related pain, a high rate of polypharmacy and increased susceptibility to the adverse effects of analgesics [6].

This chapter will review the nonpharmacological, pharmacological and surgical therapy for osteoarthritis of the knee and hip with specific reference to older people.

DIAGNOSIS AND CLINICAL FEATURES

The pain of osteoarthritis is usually activity-related. Patients with knee involvement may report that their legs "give way", which is known as instability symptom. With knee osteoarthritis, tenderness at the junction of the femur and tibia or an effusion may be present. Varus (bowlegged) or valgus (knock-kneed) deformity usually signifies marked malalignment which these changes are risk factors for worsening radiographic disease and functional limitations [7]. One of the useful signs for recognising osteoarthritis of the hip is pain that is aggravated by internal or external rotation of the hip while the knee is in full extension [8].

Blood tests are usually not indicated in the evaluation of chronic knee or hip pain unless clinical features are suggestive of rheumatoid arthritis or other forms of inflammatory arthritis. Radiological imaging is required in the workup if pain is nocturnal or not related to activities. In people with osteoarthritis, radiological findings do not correlate well with the severity of pain and radiographs of the affected joint may even appear normal in people with the condition [9].

NONPHARMACOLOGICAL INTERVENTIONS

Nonpharmacological measures have an important role in the management of osteoarthritis-related pain and disability in the older population if medication adverse effects and polypharmacy are to be avoided. The American College of Rheumatology (ACR) recommends that management of osteoarthritis should include measures such as self-management programs, social support, weight loss and appropriate footwear [10].

Both the ACR and the Osteoarthritis Arthritis Research Society International

(OARSI) recommend using lateral-wedged insoles for osteoarthritis [8, 11]. Lateral-wedged orthotics decreases the degree of varus misalignment at the knee [12]. Randomized controlled trials have shown that lateral wedged orthotics in knee osteoarthritis can decrease oral analgesic use at 6 months and 2 years but no improvement in pain or function was observed [13, 14]. However the long-term effects of this approach are currently unknown. Since an insole is a simple and inexpensive measure, lateral wedged orthotics are an option in ambulating older people with knee osteoarthritis who need to reduce non-steroidal anti-inflammatory drugs (NSAID) use.

A systematic review evaluating patellar taping in knee pain with varus malalignment found that pain was significantly reduced but only three studies included older people [15]. However further work is required to determine the efficacy of patellar taping in knee osteoarthritis.

Physical therapy to strengthen muscle function and aerobic exercises can improve osteoarthritis symptoms [16]. A systematic review of 12 randomized controlled trials (RCTs) showed that exercise therapy and manual joint mobilisation was superior to either strength training or exercise therapy alone in medial knee osteoarthritis, but all three modalities improved physical function and pain [17]. Physical therapy is even more important in older people with multiple comorbidities and requires rehabilitation.

Obesity has been considered the single most “modifiable” risk factor knee osteoarthritis [18, 19]. A meta-analysis has shown that weight loss of 5% within a 20-week period is associated with pain and functional improvement in knee osteoarthritis [20]. However the effectiveness of this approach in older people with osteoarthritis have not been examined in light of potential adverse outcomes associated with weight loss in this age group [21].

PHARMACOLOGICAL THERAPY

Oral Analgesics

NSAID is effective in treating pain as well as reducing joint swelling and stiffness in osteoarthritis and is considered the first-line treatment for mild to moderate

CHAPTER 10

Towards Unbreakable Old Bones: Osteoporosis in Older Adults

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Abstract: Osteoporosis is characterised by bone demineralisation, reduction in bone mass and changes in bone micro-architecture or the presence of a fragility fracture. Osteoporosis is still frequently underdiagnosed and undertreated. Advancing age is a risk factor for underdiagnosis and undertreatment of osteoporosis. The goal of treatment is to reduce morbidity and mortality associated with the first fracture and prevent subsequent fractures. Osteoporosis management in older adults (≥65 years of age) must involve both non-pharmacological and pharmacological interventions. Beneficial non-pharmacological interventions include falls risk assessment and management, participation in exercise programs and the use of hip protectors. Pharmacological treatments including calcium, vitamin D, bisphosphonates, denosumab, strontium and teriparatide are generally safe for use in older people and significantly reduce fracture risk especially vertebral fractures. However the evidence is not as strong for reducing the risk in non-vertebral and hip fractures.

Keywords: Bisphosphonate, Bone loss, Calcium, Denosumab, Falls prevention, Fractures, Older people, Osteoclast, Osteoporosis, Parathyroid hormone, Strontium, Vitamin D.

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INTRODUCTION

Osteoporosis is characterised by the loss of bone mass and micro-architectural deterioration of bone resulting in enhanced bone fragility and increase in risk of fracture. Osteoporosis is closely linked with aging because as people age, bone resorption by osteoclasts is not fully restored with bone deposition by osteoblasts leading to bone loss. The prevalence of osteoporosis is increasing because of extended life expectancy and an ageing population.

Worldwide, epidemiological data have shown that the annual incidence of fragility fractures increases with age [1]. In Australia, approximately 75,000 fragility fractures occur annually which includes about 21,000 hip fractures [2]. Fragility fractures are associated with significant disability, mortality and costs [3]. The burden of fragility fractures is expected to rise with an ageing population [2, 4]. Worldwide, 85% of residents in aged care facilities (RACFs) are reported to have osteoporosis [5] and approximately 40% of all hip fractures occur in this population [6].

This chapter will review changes in the bone with increasing age, diagnosis of osteoporosis, prevention of fragility fractures in older people and advances in osteoporosis treatment.

CHANGES IN BONE AND GAIT STABILITY WITH AGING

The decline in cancellous bone mass in humans begins in the third decade while loss of cortical bone starts after 50 years of age [7]. In women, bone loss occurs at a faster rate after menopause because of skeletal involution associated with estrogen deficiency. The important pathogenetic mechanism in age-related bone loss appears to be impaired bone formation attributed to decline in osteoblast numbers. This deterioration is thought to be due to a decline in the number of mesenchymal stem cells, defective proliferation or differentiation of progenitor cells, or diversion of these progenitor cells toward the adipocyte lineage, and also to increased apoptosis [8].

Age-related bone loss is largely a result of senescence mechanisms that affect bone cell number and function. These mechanisms can relate to intrinsic

senescence processes, alterations in endogenous anabolic factors and changes in local support [9, 10]. Intrinsic senescence mechanisms include telomere shortening, accumulation of oxidative stress, impairment in DNA repair and altered epigenetic processes that regulate gene expression [8]. Extrinsic mechanisms of bone senescence include deficiency in sex-hormone, decreased physical activity, nutritional deficiency and alcohol consumption or smoking [11]. Local disruptions include among others, altered signalling pathways and cell-cell communication as well as signal dysregulation in osteogenic niches [12].

Both trabecular and cortical bone are affected by these age-related changes. Based on its pathophysiology and affected regions, osteoporosis has been classified into two types: postmenopausal osteoporosis and senile osteoporosis.

DIAGNOSIS

Apart from fragility fracture being a characteristic feature of osteoporosis, diagnosis is dependent on bone mineral density (BMD) measurement with a dual-energy X-ray absorptiometry (DXA). For women, the World Health Organization (WHO) and International Osteoporosis Foundation (IOF) have identified four diagnostic groups for DXA which is used to guide treatment (Table **1**) [13].

Table 1. World Health Organisation and International Osteoporosis Foundation dual-energy X-ray absorptiometry assessment diagnostic categories.

Category	T-Score of Hip Bone Mineral Density
Normal	≥-1.0
Osteopenia (low bone mass)	<-1.0 and >-2.5
Osteoporosis	≤-2.5
Severe osteoporosis (established osteoporosis)	≤-2.5 and presence of at least one fragility fracture

T-score is the number of standard deviations below the mean value of the young healthy population.

Two risk assessment tools are available to facilitate the assessment of fracture risk in the community-dwelling population. The FRAX [14] and the Garvan [15] fracture risk assessment tools have been useful in identifying people at risk of osteoporosis and determining the threshold for treatment. However the applicability of these tools among residents of RACFs remains unknown.

CHAPTER 11

Keep the Kidneys Functioning Till the End: Chronic Kidney Disease in the Older Population

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Abstract: With population ageing and increasing life expectancy, the prevalence of chronic kidney disease (CKD) is rising. In addition to its associated cardiovascular risk, CKD in older people have increased prevalence of geriatric syndromes such as cognitive and functional decline, leading to frailty and disability. Clinical trials evaluating treatment for CKD have usually excluded patients older than 70 years, making it difficult to translate current therapeutic recommendation to the older population. Available evidence suggests that patients over 75 years of age with CKD in the presence of multiple comorbidities have greatly reduced life expectancy and quality of life, even if they choose to have renal replacement therapy. Therefore offering a conservative approach to management supported by palliative care is a more reasonable option for some patients. Kidney transplantation can lead to better life expectancy and quality of life in older people if selected carefully. There is a need for the inclusion of older people in future CKD trials so that evidence-based therapies can be offered to this group.

Keywords: Albuminuria, Creatinine, Chronic kidney disease, Dialysis, End-stage kidney disease, Geriatric syndromes, Glomerular filtration rate, Kidney transplantation, Palliative care, Renal replacement therapy.

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INTRODUCTION

The proportion of older people (aged >65 years) is steadily increasing worldwide, with rapid growth seen in low and middle-income countries. This demographic change has important implications for health conditions such as chronic kidney disease (CKD), for which the prevalence increases with age.

It is well recognised that estimated glomerular filtration rate (eGFR) declines with increasing age [1]. Relative increases in the prevalence of CKD with age have been reported in the U.S., Canada, China, U.K. and European countries [2]. Furthermore the incidence of dialysis-dependent kidney disease has steadily increased among older people. For example, in the U.S., a 57% age-adjusted increase in the number of octogenarians and nonagenarians starting dialysis was observed between 1996 and 2003 [3].

CHANGES IN THE KIDNEYS WITH INCREASING AGE

Kidney function declines as a normal part of ageing and some of the causes were shown in (Table **1**) [4]. Renal mass decreases with age, secondary to a reduction in the number of glomeruli [1]. It used to be thought that GFR inevitably declined with age, but longitudinal studies now suggest that in about one-third of patients, there is no significant decrease in renal function, even up to the age of 89 years [5, 6]. However, co-morbidities which are prevalent in older people, such as hypertension, cardiovascular disease, and diabetes mellitus, can significantly impact kidney function [7]. The underlying causes of renal failure may not be immediately apparent in some cases because the definitive diagnostic test, renal biopsy, sometimes carries greater risks than benefits in the older population.

Table 1. Kidney changes with increasing age.

1. Decreased size by 20–30% by the age of 70 years
2. Decline in length, number, and thickness of renal tubules
3. Interstitial tissue and tubular diverticula of renal tubules are increased
4. Decrease in renal blood flow by approximately 10% per decade after the age of 20 years
5. Glomerular filtration rate decreases about 10 mL/min per decade
6. Free water absorption decreases by about 5% per decade after the age of 50 years
7. Decrease in effective renal plasma flow is proportionally greater than glomerular filtration rate
8. Accelerated decline in kidney function in the presence of conditions such as hypertension, atherosclerosis, and heart failure

ASSESSING KIDNEY FUNCTION IN OLDER PEOPLE

The Kidney Disease Improving Global Outcomes (KDIGO) published in 2013 did not provide specific recommendations on the early identification and management of CKD in older people [8]. In fact, the current classification may overestimate the prevalence of CKD in the older population [9]. Within the new classification system, age-related cut-off points for the diagnosis of CKD are no longer recommended [10]. This change was based on evidence that reduced eGFR and albuminuria predicted End-Stage Kidney Disease (ESKD) onset and mortality, irrespective of age [11].

Creatinine is not a sensitive marker of kidney function because it can be affected by muscle mass, diet and renal tubular secretion [12]. As a result measurement and reporting of kidney function has evolved from using serum creatinine to complex formulae such as the Cockcroft-Gault [13], Modification of Diet in Renal Disease (MDRD) [14] and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations [15]. KDIGO currently uses the CKD-EPI formula because it is considered to be more accurate [8]. However it remains unclear how accurate these formulae are in older people and one study have found these equations may misclassify CKD by one stage [16]. To our knowledge, frailty status has not been explicitly considered in validation studies of equations estimatingGFR. However, since sarcopenia is a core feature of the frailty phenotype [17], GFR estimated from plasma creatinine may overestimate the true GFR for older people who are frail.

All creatinine-based equations for estimating eGFR contain an age variable. As age is a strong factor predisposing to all-cause mortality and cardiovascular morbidity and mortality, it can confound the observed relationship between eGFR and these outcomes. Measuring urine albumin excretion might help clarify which older person truly has CKD and is at increased risk for disease-related adverse events [18].

BURDEN OF CKD IN OLDER PEOPLE

In the UK, the prevalence of CKD in people ≥75 years old is 56.1% for eGFR <60, 17.7% for eGFR <45 mL/min/1.73 m^2 and 2.7% for eGFR <30 mL/min/1.73

CHAPTER 12

End of Life Care in Older People

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Abstract: The end-of-life support older people receive is an important aspect of high quality health and social care, especially for those with chronic diseases. To provide high-quality end-of-life care, it is important to clarify with patients their values and goals in treatment through advanced care planning. Such an approach improves the concordance between expressed preferences for care and delivery of care as well as the satisfaction with care. Available research indicates that majority of older people would like the opportunity to discuss their end-of-life care but there are still barriers to such conversations. End-of-life care of older people with chronic diseases should focus on identifying and treating symptoms. Therefore, in end-of-life care, medications which are not intended for symptom control should be avoided.

Keywords: Advance care planning, Carers, Decision-making, Dying, End-of-life, Palliative care, Quality of life, Resuscitation, Terminally ill, Treatment withdrawal.

INTRODUCTION

Supporting older people towards the end of their lives is an important part of high quality health and social care. People are living longer with a high prevalence of multiple chronic diseases and frailty resulting in a growing population requiring complex support even at the end of their lives.

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Therefore providing end-of-life care for the older population often involves ethically and medically challenging decision-making which requires health professionals to carefully consider patients' multiple comorbidities, their quality of life and their wishes regarding treatments.

In general, end-of-life is characterised by health problems accumulating over a period of weeks to months with irreversible pathophysiological changes which leads inevitably to death. Recognizing this end-of-life phase can be challenging for many health professionals and usually requires repeated evaluations over a period of several days or even weeks. The terminal phase of illness indicates that death is imminent, generally within hours or days. Therefore, end-of-life can be viewed as the broader continuum of the terminally ill state.

For health professionals, providing good quality end-of-life care can be challenging and complex. Even with widespread professional acknowledgment of the importance of palliative care, clinicians are often unaware of patients' wishes regarding end-of-life care, interventions are often inconsistent with patients' preferences, and some patients still die in moderate or severe pain [1, 2]. Technology-filled end-of-life care is often associated with reduced quality of life, lower satisfaction of care and increased anxiety for carers and families [3].

This chapter will look at the attitudes of the public and clinicians to advance care planning discussions in older and frail people. In addition, it will also review general aspects of end-of-life care and the prescription of medications for older people in this setting.

RECOGNISING END-OF-LIFE

For a long time, clinicians have recognized that there are circumstances in which patients can no longer benefit from, or do not wish to continue with the burdens of life-sustaining therapies. With their medical expertise and advocacy for patients, physicians have an important responsibility to share clinical prognoses with their patients and families.

Before any good-quality plans for end-of-life patients can be implemented, it is important to first recognise end-of-life itself. A number of symptoms and signs

indicating end of life are shown in Table **1** [4].

Table 1. Signs and symptoms indicative of end-of-life.

1. Dependent for all activities of daily living; requiring assistance of caregivers to survive; urine and faecal incontinence
2. Severe impairment of expressive and receptive communication often limited to single words or nonsense phrases
3. Eating or feeding difficulties; loss of ability to recognise food, self-feed, swallow effectively; refusal to eat and drink with weight loss; persistent inability to eat when fed
4. Loss of ability to walk followed up by inability to stand, problems in maintaining sitting posture and subsequently loss of head and neck control, eventually bed bound
5. Development of contractures because of muscle rigidity and deconditioning
6. Persistent confusion, agitation, withdrawal, lethargy or apathy
7. Recurrent infections
8. Having no recognition of family/friends/everyday objects

Adapted from Recognise End of Life and Care Holistically (REACH) toolkit [4].

THE PUBLIC'S ATTITUDE TO END-OF-LIFE CARE DISCUSSIONS

A number of studies have consistently reported that between 61% and 91% of older people would like to discuss their end-of-life care [5 - 9]. Older people saw the benefits of discussions to include assurance that their wishes would be taken into consideration, the opportunity to address important issues of care before developing cognitive impairment or serious illnesses [6]. However there are also studies indicating some older people preferring to 'live one day at a time' [10] and postpone making plans until they were older or in worse health [11].

Most older people wanted discussions on end-of-life care sooner rather than later [7 - 9, 12]. These participants perceived the risk of 'leaving it too late' and recognized the benefits of early discussions would outweigh any discomfort [8]. However there are studies reporting that some older people would defer such discussions till the onset of a terminal or debilitating illness triggering the need for such plans [11, 13].

ARE END-OF-LIFE CARE DISCUSSIONS BEING HELD?

Studies have found that only 2-29% of frail older people had discussed and made some form of end-of-life care plans with a healthcare professional [12, 14 - 16]. There is also often disparity between conversations that patients have held with

Closing Remarks: Chronic Diseases In Geriatric Medicine

The prevalence of chronic diseases in the older population aged ≥65 years has generally increased over time [1, 2]. One of the key questions is whether an increase in life expectancy is accompanied by a concurrent postponement of functional limitations and disability. One of the challenges in older people is the need to manage multiple coexisting chronic diseases.

Multiple coexisting chronic diseases in an individual increase sharply with age, affecting about two-thirds of people aged 65 years and older [3 - 5]. Older patients with multiple chronic diseases experience lower quality of life, disability, dependence and increased hospital admissions [3, 6, 7]. As a result care coordination is essential to meet challenges arising from older people with multiple chronic diseases. Rigid application of clinical practice guidelines intended for single disorders should also be avoided to minimise adverse drug reaction, polypharmacy and unnecessary cost [8].

In older people, comprehensive geriatric assessment provides an important structured framework within which clinicians can integrate holistic assessment and treatment in the presence of complex comorbidities [9]. This is particularly important among frail older people who often also have multiple complex chronic conditions. Frailty often coexists with many chronic disorders because of common risk factors or underlying pathophysiologies, or because one disorder is a complication of another, or its treatment [10].

To meet the needs of older people with chronic diseases, social and economic inequalities in access to health care have to be eliminated. To achieve these needs, age discrimination should be countered and the challenges posed by multiple chronic diseases addressed. As discussed in this book, age discrimination is apparent in primary and secondary prevention of cardiovascular disease and treatment of stroke [11 - 13]. In cancer care among older people, fewer diagnostic and staging procedures are done and less evidence-based treatment is given to older people, even after taking frailty into account [14]. Even for drugs frequently prescribed in older age, older people tend to be excluded from clinical trials that would generate evidence to inform their treatment [15]. These barriers need to be overcome to better meet the needs of older people with chronic illnesses.

A substantial proportion of morbidity and mortality due to chronic diseases occurs in older people. Primary prevention in adults younger than 60 years will improve health in their older age, but much of the potential to reduce disease burden will come from effective primary, secondary and tertiary prevention targeting the older population. Although population ageing

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is driving the worldwide epidemic of chronic diseases, substantial untapped potential exists to modify the relation between chronological age and health.

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SUBJECT INDEX

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