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Clinical management of older persons with haemophilia

C. Hermans [a,*,1], P. de Moerloose [b,1], G. Dolan [c,1]

[a] Haemostasis-Thrombosis Unit, Division of Haematology, Cliniques Universitaires Saint-Luc, Brussels, Belgium
[b] Hemostasis Unit, University Hospital and Faculty of Medicine, Geneva, Switzerland
[c] Nottingham Haemophilia Comprehensive Care Centre, Nottingham University Hospitals, Queens Medical Center, Nottingham, UK

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Abstract

Life expectancy for people with haemophilia (PWH) has improved and is now approaching that of the general population. The growing population of elderly PWH will therefore increasingly face the age-related morbidities such as cardiovascular diseases, malignant disease, liver disease, and bone and joint related diseases, as well as the lifestyle and psychosocial factors that accompany many of these conditions. For many PWH, frequent contact with haemophilia specialists within the comprehensive care centres supplants the relationship that individuals in the general population have with their general practitioners. As a result, there is a risk that elderly PWH may miss the chronic disease screening opportunities offered to the general population. This review focuses on the screening tests and examinations recommended for age-related comorbidities in the general population that may be applicable to the growing population of older people with haemophilia.

Keywords: Haemophilia; Comorbidity; Ageing; Cardiovascular disease; Cancer

1. Introduction

Since the introduction of effective replacement therapy and the institution of comprehensive care, the management of haemophilia has become a complex discipline that focuses not only on treatment but on the provision of holistic care by a multidisciplinary team [1]. Substantial improvements in health and quality of life have been achieved through prevention of bleeding, long-term management of joint and muscle damage and the avoidance and management of complications from treatment.

Consequently, life expectancy for people with haemophilia (PWH) has improved and is now approaching

* Corresponding author.
E-mail address: cedric.hermans@uclouvain.be (C. Hermans).
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that of the general population [2]. The result at a societal level is that there are many more older PWH than in previous generations. This presents new clinical challenges [3,4], particularly in managing age-related morbidities such as cardiovascular disorders, malignant disease, liver disease, bone and joint related diseases, neurological conditions such as dementia, as well as lifestyle issues such as obesity and physical activity, sexual difficulties, depression and psycho-social issues. These are mostly conditions that, in the general population, are managed by generalists or by specialists with little training in haemophilia; little is known on how to manage such comorbidities in the specific context of haemophilia, an issue not yet addressed in haemophilia guidelines. There is evidence that PWH fare better when haemophilia is managed by specialists rather than by generalists, particularly when care is delivered within comprehensive haemophilia treatment centres (HTCs) rather than delivered by community-based physicians [5].

As a chronic condition, haemophilia should be monitored constantly and periodically reviewed in the light of the patient's clinical progress. Those with severe haemophilia should be assessed at least annually while those with mild and moderate disease may be reviewed less frequently. Although there is as yet no consensus at a European level, previous publications such as those of the European Haemophilia Therapy Standardisation Board (EHTSB) have made recommendations regarding haemophilia specific information that should be captured at each review, mainly relating to haemophilia treatment, inhibitor status, bleeding phenotype, joint status and pain, major co-infections (HIV and HCV) and dental care [6]. The present paper focuses on the additional screening tests and examinations recommended for age-related comorbidities in the general population that may be applicable to the growing population of older people with haemophilia and which may require closer liaison with and referral to health care professionals in other specialties.

2. Screening for and management of comorbidities in elderly PWH

In order to facilitate comprehensive follow-up care for older people with haemophilia, it is important that the clinical record contains adequate documentation of information in at least five core clinical domains:

- Cardiovascular disease (CVD)
- Cancer
- Liver disease
- Osteoporosis
- Lifestyle and psychosocial issues.

The relevant parameters that should be captured and monitored as well as the relevant tools to do so are detailed here for each of these domains.

2.1. Cardiovascular disease

Diseases of the heart and circulatory system are the main cause of death in Europe, accounting for over 4.3 million deaths each year [7]. Nearly half (48%) of all deaths are from CVD, the main forms of which are coronary heart disease (CHD) and stroke. Just under half of all deaths from CVD are from CHD and nearly a third from stroke. Cardiovascular risk arises from the contributions of a number of cardiovascular risk factors, including smoking, diabetes, elevated blood pressure, low physical activity and elevated serum cholesterol. Risk equations such as SCORE and QRISK have been developed and validated to predict risk with a reasonable degree of accuracy based on risk factors such as gender, age, lipid profile, systolic blood pressure, family history of premature cardiovascular disease, smoking status and renal failure [8–10]. Concerning renal disease it has to be noted that in the general population the incidence is principally linked to ageing and is frequently secondary to other chronic conditions, such as hypertension and diabetes [11,12]. The cause of death in case of end stage renal disease (ESRD) is a cardiovascular event in 46% of cases [13].

Data from cohort studies suggest that PWH have lower cardiovascular mortality rates compared with the general population [14,15]. This has often been taken to suggest that haemophilia confers a protective effect against cardiovascular disease. In a Dutch retrospective analysis of medical records of patients born before 1971 has shown a reduced incidence of myocardial infarction among those with severe haemophilia compared with age-matched controls in the general population, suggesting a protective effect of very low clotting factor levels on thrombotic cardiac events [16]. However, imaging studies based on assessment of coronary artery calcification score and carotid intima-media thickness in patients with haemophilia suggest that the extent of atherosclerosis is comparable between elderly men with and without haemophilia [17,18]. It may be, however, that severe haemophilia protects against acute ischaemic events, with this protection being unmasked by replacement therapy. Furthermore, haemophilia confers no protection against the longer term effects of risk factors such as hypertension, hypercholesterolaemia and hyperglycemia, which also enhance the risk of microvascular disease and cerebral haemorrhage. These may include peripheral arterial disease (PAD), a marker for systemic atherosclerosis and ischaemic risk that shares similar risk factors with other cardiovascular diseases [19], and renal disease.

As with the general population, PWH acquire risk factors for cardiovascular disease with advancing age [20–22]. A cohort study in Italy found that elevated blood pressure was more common in PWH compared with age-matched peers after adjusting for alcohol intake, use of pain killers and anti-HIV medication [23]. A large cross-sectional study of Dutch and British patients aged ≥30 years indicated that the prevalence of hypertension (blood pressure ≥140/90 mmHg) was significantly higher in haemophilia patients than in