ELECTIVE (SSC5c) REPORT (1200 words)

A report that addresses the above four objectives should be written below. Your Elective supervisor will assess this.

OBJECTIVE 1: WHAT IS THE PREVALENCE OF ISCHAEMIC HEART DISEASE IN THE UK AND HOW DOES THIS COMPARE TO OTHER COUNTRIES IN EUROPE?

According to the World Health Authority, cardiovascular disease (CVD) "causes 46 times the number of deaths and 11 times the disease burden caused by AIDS, tuberculosis and malaria combined in Europe" and carries the highest disease mortality [1]. Mortality of CVD in Europe can be broken into that due to coronary artery disease (20/21%), stroke (10/15%) and "other CVD" (12/16%) for men/women respectively [2]. For the purposes of this work, we will consider coronary artery disease (CAD) and ischaemic heart disease (IHD) to be equivalent [3].

In the UK, CVD has a prevalence of over 3 million people with annual treatment costs exceeding £30 billion; CAD is the main component of CVD and accounts for approximately 95,000 deaths per year [4]. UK mortality rates for CAD have been falling over time and are now 20% of their age-specific levels compared to 1968 [5]. The age-adjusted prevalence of heart disease over Western and Northern Europe in 2004 ranged from a low of 9.5% for Switzerland to a high of 20.3% for Sweden (England: 19.0%, France 19.3%) [6]. However, in Eastern Europe and former member countries of the USSR a rising pattern in mortality due to CAD is seen, where, notably, "the highest mortality rates ever recorded are currently being observed"; while, in contrast, Mediterranean Europe generally shows non-increasing rates [7]. In the European Union, the annual cost of CAD is approximately is €60 billion [8].

OBJECTIVE 2: HOW ARE NON-INVASIVE CARDIAC IMAGING SERVICES ORGANISED AND DELIVERED BY THE INSTITUTE AND ARE THERE ANY SIGNIFICANT DIFFERENCES BETWEEN THIS COMPARED TO ELSEWHERE IN THE UK OR IN EUROPE?

Delivery and organisation of cardiac imaging services in both the UK and Europe is based on national guidelines, local policy, and patient and clinician choice. The National Institute of Health and Clinical Excellence (NICE), British Cardiovascular Society and the European Society of Cardiology set standards and provide guidelines [9].

At the national level in the UK, NICE guidelines are followed: the choice of modality follows a full clinical assessment and depends on the likelihood of CAD. A non-invasive approach is most cost effective if this likelihood is 30-60%, while invasive coronary angiography is the first-line investigation above this; for 10-29% CT scanning with calcium scoring is proposed [10]. Assessment of the likelihood of CAD is detailed in Clinical Guidance 95 (CG 95) [11]: this is based on age, the nature of the chest pain and a classification into high (presence of diabetes, smoking and hyperlipidaemia) or low risk.

The European Society of Cardiology (ESC) "publishes guidelines and recommendations for clinical practice […] across Europe and in all areas of cardiology" [12]. One set of guidelines relevant here are the "2013 ESC guidelines on the management of stable coronary artery disease" (ESC2013). These recommend a stepwise approach: determine the likelihood of stable CAD; diagnose with non-invasive testing; and implement optimal medical therapy [13]. In ESC2013, stratification on pre-test probability (PTP) is: <15% exclude other causes of chest pain; 15-85% undertake further non-invasive testing; and

>85% the diagnosis is primarily clinical. The choice of modality is based on the PTP, availability, local expertise, and patient criteria and suitability.

At the level of service delivery, the same factors come into play in the UK and Europe: "The choice of non-invasive functional imaging test will be determined by local availability and expertise, relevant contraindications and patient preferences" [10]. At national level, some differences can been seen between NICE CG 95 [11] and the 2013 ESC guidelines [13], the latter guideline being extremely comprehensive. While both use pre-test probabilities to determine imaging modality, formally different algorithms are used to compute these (although this does not suggest that a difference in clinical outcome would result).

The cardiology imaging services delivered by the Barts Health Centre include computed tomography (CCT), magnetic resonance imaging (CMRI) and nuclear medicine (CNM) [14].

OBJECTIVE 3: WHAT IS THE EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY OF ISCHAEMIC HEART DISEASE?

The epidemiology of ischaemic heart disease is discussed in objective 1. The aetiology of CAD is typically divided into modifiable (age, gender, genes) and non-modifiable factors (such as lifestyle and environment) [1, 15]. Increased age, male gender, social deprivation, smoking, poor nutrition, reduced physical activity and increased body mass index, increased alcohol intake, abnormal blood lipid levels, raised blood pressure, type 2 diabetes, positive family history and specific ethnicities all increase the risk [1, 15]. Factors such as high blood pressure and cholesterol levels are influenced by both genetic and lifestyle factors. One highly influential investigation into the epidemiology of coronary heart disease is the Framingham Study [16] which looked at many of the above risk factors: interestingly in this a number of factors were found to be unrelated to the incidence of CAD, such as marital status, coffee, sleep, level of alcohol consumption and socioeconomic status while the last two are now considered to be more relevant [15].

CAD is an inflammatory disorder where the coronary arteries are occluded by fatty and calcified plaques. Formation of an atherosclerotic lesion results from an initial insult to the artery lumen: subsequent leukocyte adhesion and migration into the intima and the resultant intercellular communication leads to the differentiation of other cell types into foam cells and the secretion of a lipid-rich extracellular matrix with a "necrotic core" due to cell apoptosis [17]. Triggers for the adhesion process are legion: examples are the pro-inflammatory cytokines produced by adipose tissue in obesity, glycosylation and oxidation from hyperglycaemia in diabetes, and vasoconstrictive processes such as found in underlying hypertension [17]. Smoking warrants a specific mention as it has many effects: it impacts the lipid profile, reduces vasodilation and leads to an overall enhancement of the inflammatory process [18]

OBJECTIVE 4: WHAT ARE THE TECHNICAL AND PRACTICAL CONSIDERATIONS INVOLVED IN UNDERTAKING NON-INVASIVE CARDIAC IMAGING IN ISCHAEMIC HEART DISEASE?

Considerations of non-invasive imaging include availability, cost, clinical appropriateness and patient choice.

Echocardiography is the most widely available (and the cheapest) while the other techniques are more expensive with variable local availability. All of the methodologies need specialists trained to undertake and interpret the imaging. Each method provides different information which guides

choice: echocardiography is suitable as a screening tool for, say, valvular dysfunction or global wall motion abnormalities while nuclear perfusion studies are the gold standard for investigating the viability of cardiac tissue [19]. Cost-benefit considerations are important: the question needs to be asked which modality is more appropriate under this filter, given the degree of clinical suspicion.

The use of contrast agents raise questions of adverse reactions. Stress testing, for example using pharmacological stressors, is contraindicated in certain patients, e.g. with severe aortic stenosis [20]. CCT involves radiation doses which may need consideration of suitability in (for example) younger patients [13]. CMRI is contraindicated in the presence of certain implants, such as ferromagnetic vascular clips [21].

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