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Cardio-oncology: where do we stand for in Belgium?

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ABSTRACT

Cardiovascular disease (CVD) and cancer represent the two main causes of death in industrialised countries. Both share common risk factors (diabetes, obesity, hypertension, diet, smoking, etc.). The associated timing of CVD and cancer onset is thus largely influenced by modifiable risk factors. Advances in cancer treatment have extended the lives of patients with cancer, but for some at the cost of adverse cardiovascular events. The rapidly growing number of patients surviving cancer, often in the setting of advanced age, new or pre-existing CV disease and risk factors, the management of these patients has become the concern of experts in cardio-oncology. The goal of cardio-oncology is to provide optimal care for patients with cancer and/or at risk of cardiovascular disease. To date, no specific cardio-oncology teaching programme is available in Belgium. The present paper reports the results of the Belgian Society of Cardiology (BSC) survey on cardio-oncology. The vast majority of respondents (154/159, 97%) are in favour of organising courses or educational meetings on cardio-oncology. A dedicated cardio-oncology clinic was present in only 40% of the hospitals that participated in the survey. Compared to the data collected by the European Society of Cardiology, the number of respondents considering themselves as experts in the management of left ventricular dysfunction or atrial fibrillation complicating cancer treatment was much lower in Belgium (11% vs. 30%).

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Heart and cancer: common risk factors

Worldwide, the total number of people alive within 5 years of being diagnosed with cancer is estimated at 43.8 million (\cong 200,000 in Belgium) [1,2]. To date, about 423 million people suffer from cardiovascular diseases, themselves associated with 17.9 million deaths [1]. In Belgium, heart disease and cancer combine to account for 31% and 23% of deaths in women and 27% and 29% of deaths in men [2,3]. Although commonly thought of as two separate disease entities, cardiovascular disease (CVD) and cancer possess various similarities and possible interactions, including a number of similar risk factors (age, obesity, diabetes mellitus), suggesting a shared biology [4,5]. The associated timing of CVD and cancer onset is thus largely influenced by modifiable risk factors. The incidence of both cancer and CVD increases with advancing age with $\frac{3}{4}$ of new cancer diagnoses occurring in individuals ≥ 55 years in developed countries ($>50\%$ in patients >70 years in Belgium) [6]. Cigarette smoking greatly impacts cardiovascular incidence and mortality,

contributing to all stages of atherosclerosis through various mechanisms [7]. Tobacco usage, particularly *smoking* ($\cong 23\%$ of Belgian inhabitants), is also a preventable and heavily weighted risk factor for multiple cancer types. Smoking is responsible for 30% of all cancer-related deaths [8]. *Hypertension* ($\cong 25\%$ of Belgian inhabitants) is a well-established CVD risk factor [9]. Hypertension is a major health problem worldwide, as it affects approximately 3 in 10 adults over age 20, leading to high morbidity and mortality. Hypertension is associated with several specific cancer types with a particularly strong association with renal cell carcinoma (1.6-fold increase) [10]. *Obesity* ($\cong 20\%$ are overweight in Belgium) represents a significant risk factor for cancer; up to 20% of all cancer may be weight-related [11]. The carcinogenic effects of obesity on sex can differ, and this is most substantial for colon cancer (55% increased risk of colorectal cancer in men than in women) [12]. The potential protective effect of elevated oestrogen levels commonly observed in obesity can, however, be counteracted by an increased risk of breast and endometrial cancer

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Table 1. Questions asked and responses received from 159 cardiologists.

Questions responses	
Your age?	
• Under 30	• 3%
• 30–44	• 40%
• 45–60	• 43%
• Over 60	• 14%
Your gender?	
• Female	• 30%
• Male	• 69%
• Prefer not to answer	• 1%
Where are you working?	
• Academic university hospital	• 47%
• Community public hospital	• 40%
• Cardiology practice	• 7%
• Other, please specify	• 6%
What is the size of your hospital?	
• <300 beds	• 4%
• 300–600	• 33%
• >600	• 64%
Do you have at your hospital a dedicated cardio oncology clinic?	
• Yes	• 40%
• No	• 60%
How many patients with a possible CV complication of cancer treatment did you see in the last 12 months?	
• None	• 3%
• 1–5	• 29%
• 5–20	• 42%
• >20	• 26%
In your professional environment where are ambulatory cancer patients with cardiovascular health problems reviewed?	
• General cardiology clinic	• 54%
• A part time single specialist Cardio-Oncology Service	• 16%
• Structured Cardio-Oncology Service with one or two dedicated specialists inside a community hospital	• 11%
• Cardio-Oncology Centre inside a large tertiary hospital	• 10%
• Cardio-Oncology Centre inside a large Oncologic specialist hospital	• 7%
• Other – please describe	• 3%
How do you judge your knowledge and skills about management of patients with left ventricular dysfunction complicating cancer treatment?	
• Scarce	• 7%
• Acceptable	• 33%
• Fair	• 49%
• Expert	• 11%
How do you judge your knowledge and skills about management and anticoagulation of patients with atrial fibrillation complicating cancer treatment?	
• Scarce	• 5%
• Acceptable	• 38%
• Fair	• 45%
• Expert	• 12%
In your specific clinical environment do you receive referrals from GPs or other specialists to evaluate a patient with cardiac problems who has received previous cancer therapy?	
• Never	• 7%
• Rarely (1–5 times/year)	• 39%
• Moderately (5–20/year)	• 26%
• Frequently (>20/year)	• 29%
Are you regularly reviewing patients with a known history of cancer treatment for CV diseases?	
• Never	• 1%
• Rarely	• 34%
• Commonly	• 65%
Did you read and apply suggestions of the 2016 ESC Position Paper on cancer treatments and cardiovascular toxicities?	
• No	• 17%
• I don't know this position paper	• 16%
• I read it but I don't apply it in my practice	• 11%
• I read it and I always apply its suggestions in my practice	• 56%
Should the BSC host educational courses or meetings on specific aspects of Cardio-Oncology?	
• No – I don't need it	• 3%
• Maybe	• 28%
• Yes	• 69%

[13,14]. The deleterious effects of *diabetes* mellitus ($\cong 6.4\%$ of Belgian inhabitants) on the macrovasculature render it a coronary heart disease risk equivalent [15]. Numerous studies link diabetes mellitus to cancer risk (as much as a 2.5-fold increased risk for certain cancers, especially in women) and its progression

(colorectal, breast, endometrial, liver, pancreatic, and bladder cancers) [16]. The role of *dietary composition* in cancer risk ranges from known carcinogens in food sources to dietary components impacting obesity, hypertension, hyperlipidaemia, and chronic inflammatory patterns that mediate cancer risk [17]. Serum lipid

levels have a well-known association with coronary artery disease [18]. *Hyperlipidaemia* as a risk factor for cancer remains inconclusive, although it appears more convincing for breast cancer and less conclusive for some other cancers [19]. High *alcohol* levels are associated with increased CVD and risk of oropharyngeal, laryngeal, oesophageal, liver, colorectal, and pre- and post-menopausal breast cancers [20]. *Inactivity* and *low-grade chronic inflammation* also increased the risk of CVD and cancer [21,22]. In Belgium, physical activity is graded insufficient in one in three adults [3]. Keeping all this in mind, priority should be thus given to targeting common risk factors and addressing comorbidities that cause these two highly morbid diseases, as this would not only reduce the burden of the disease, but would be potentially cost-effective.

Cardio-oncology service

Advances in cancer treatment have extended the lives of patients with cancer, but for some at the cost of adverse cardiovascular events [23,24]. Increasing age, underlying heart disease, and other comorbidities are contributing factors [14]. Cardiovascular complications from cancer therapy have become a leading cause of morbidity and mortality in cancer survivors. Compared with relatives, cancer survivors are 10 times more likely to develop coronary artery disease, heart failure, or a cerebrovascular event [25]. Among survivors with any type of cancer diagnosed before the age of 55 years, the risk of cardiovascular death is more than ten-fold greater than in the general population [26,27]. The risk of death from CVD is several times (2 to 6-fold) that of the general population in the first year of diagnosis; this risk increases as survivors are followed for ten years or more. Cancer has thus to be considered an independent risk factor for CVD [28]. As a result, the medical community is increasingly concerned about the cardiovascular health of cancer patients. Screening for cardiovascular risk factors and anti-cancer-related complications by dedicated care providers has thus been advocated [29]. The origins of cardio-oncology date back late in the 1960s, when cardiac dysfunction resulting from anthracyclines was first recognised as an important side effect. The field since then has arisen in few centres, and in the past years has rapidly evolved and become more a formal subspecialty with smaller units emerging within major centres [30]. *Cardio-oncology* is a burgeoning cardiology discipline, clinically focussing on the cardiovascular care of patients with active cancer, patients treated with cancer therapies associated with CVD risk,

and prevention and treatment of CVD in cancer survivors. The ultimate goal is to provide optimal care for patients with cancer and/or at risk of CVD. Cardio-oncology services are conceived as an alliance of dedicated professionals, to provide multidisciplinary specialised evaluation and consistent, continuous, coordinated and cost-effective care, during the cancer process. The early recognition of the cardiac side effects of anti-cancer agents and radiation therapy, balanced with the knowledge of the natural history of the malignancy and the benefits of oncologic treatments, is known to offer the greatest opportunity for long-term disease-free survival [31–33]. The establishment of a training and education programme in cardio-oncology has thus become a priority for the cardiology and oncology community (oncologists, haematologists, radiotherapists) [34].

Belgian Society Cardiology survey on cardio-oncology

Cardio-oncology practice requires a complex organisation that may differ substantially among hospitals and communities [29,30]. Little is known about the current knowledge, service structure and the activity of cardiologists looking after cancer patients in Belgium. Consequently, the Belgian Society of Cardiology (BSC) decided in 2019 to extend the survey carried out by the European Society of Cardiology (ESC) Cardio-Oncology Council, in which very few Belgian centres had participated. The survey was sent out to 606 members of the BSC. A total of 159 responses were collected, representing 26.2% of the population who received the questionnaire, which was significantly higher than that of the European Council (Table 1). The majority of respondents were between 30 and 60 years old (83%). Males were more represented than females (69% vs. 31%). Most of the participants worked in an academic university hospital (47%) or in a community public hospital (40%). A dedicated cardio-oncology clinic was present in only 40% of the hospitals. In response to how many patients with possible cardiovascular complication of cancer treatment were seen in the previous 12 months, 74% of the respondents had seen between 1 and 20 patients while 26% had seen over 20 patients. About 54% of the respondents worked in general cardiology clinic, 16% as a part time with only 3% working in dedicated cardio-oncology centres in specialist cancer hospitals. The majority of respondents rated their knowledge as 'fair' for their management of patients with common cardiovascular conditions such as LV dysfunction

Should the BSC host educational courses or meetings on specific aspects of Cardio-Oncology?

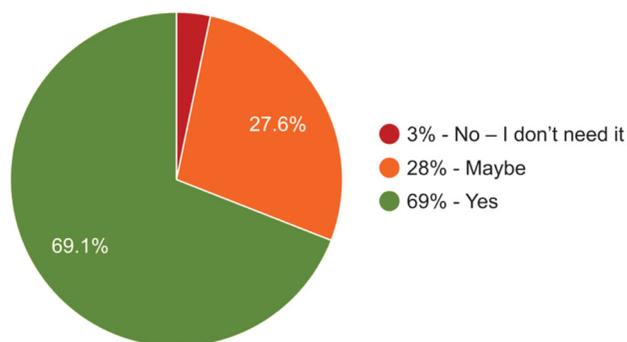


Figure 1. Responses to 'should the BSC host educational courses or meetings on specific aspects of Cardio-Oncology?'.

(49%) and atrial fibrillation (45%) with around 11% rating themselves as experts in managing these patients with a much smaller number rating their knowledge as 'poor' (5–7%). Compared to the data collected by the ESC, the number of experts (11% vs. 30%) is much lower. About 29% of respondents stated to receive more than 20 referrals annually from General Practitioners. Respondents (65%) regularly reported seeing cardiovascular patients with a known history of cancer. Intriguingly, 44% of the respondents were not aware or did not use the 2016 ESC position paper on the management of cancer patients. When asked if the BSC should host educational courses or meetings on cardio-oncology, an overwhelming majority responded positively (97%) with a strong yes in 69% and a maybe in 28% (Figure 1). To date, no specific cardio-oncology teaching programme has been organised in Belgium, whereas our neighbours (France, Italy, Netherlands) have developed one a few years ago. It should be noted that although this survey is the first on the subject in Belgium, the data collected did not allow a precise analysis of the frequency of the practice of cardio-oncology.

Conclusions

The management of cancer patients at risk or suffering from cardiovascular complications remains complex and requires a multidisciplinary approach. In the absence of an education programme in this area, Belgium remains behind its neighbours. Few Belgian cardiologists consider themselves experts in the field and few clinics dedicated to cardio-oncology are available. To fight CVD in cancer patients, the BSC has launched a new Cardio-Oncology Council in order to inform doctors on the prevention and management of CVD related to cancer treatments and radiotherapy. A

specific research grant from the Belgian Heart Foundation has also been created to promote research in this area.

Disclosure statement

No potential conflict of interest was reported by the authors.

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