6 CARDIOVASCULAR DISEASE AND FEMALE SEXUAL DYSFUNCTION

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INTRODUCTION

Female sexual dysfunction (FSD) is age related and has been shown to be common among women with cardiovascular disease (CVD) (1-3). Sexual activity is an important component of quality of life in both patients with CVD and their partners, including many elderly patients (4). Interestingly, according to the National Health and Social Life Survey more women (43%) than men (31%) reported sexual problems (5). After a cardiovascular event, the psychological impact as well as the physiological effects of the disease and the medications prescribed after an event can have a major effect on patients' sexual life. Furthermore, patients or partners' anxiety of another cardiac event often lead to reduced sexual activity or sexual dysfunction (6) (7) (8).

Male sexual function received close scientific attention, as erectile dysfunction was shown to be an independent risk factor for future cardiovascular events (9;10). However, FSD related to CVD remains under explored.

A recent survey among Dutch cardiologist (n=414) showed that cardiologists inform less often about sexual function in women than in men ($p<0.001$)(11). Subsequently, a consensus document from the American Heart Association was published, encompassing recommendations for healthcare professionals regarding sexual counseling and routine assessment of sexual problems in patients with CVD and especially those after a cardiovascular event (12). Male and female patients are being addressed together in these guidelines, while studies evaluating experiences and needs of women with CVD regarding sexual healthcare have not yet been performed.

We hypothesized that women with CVD have different expectations and demands than men regarding sexual healthcare in cardiology. Therefore, the aim of this study was to evaluate views of female cardiac patients with regards to sexual healthcare, in a multi-centered sample of women consulting the cardiologist. Results provide the necessary information to offer effective patient- centered care for female patients in cardiology practice.

METHODS

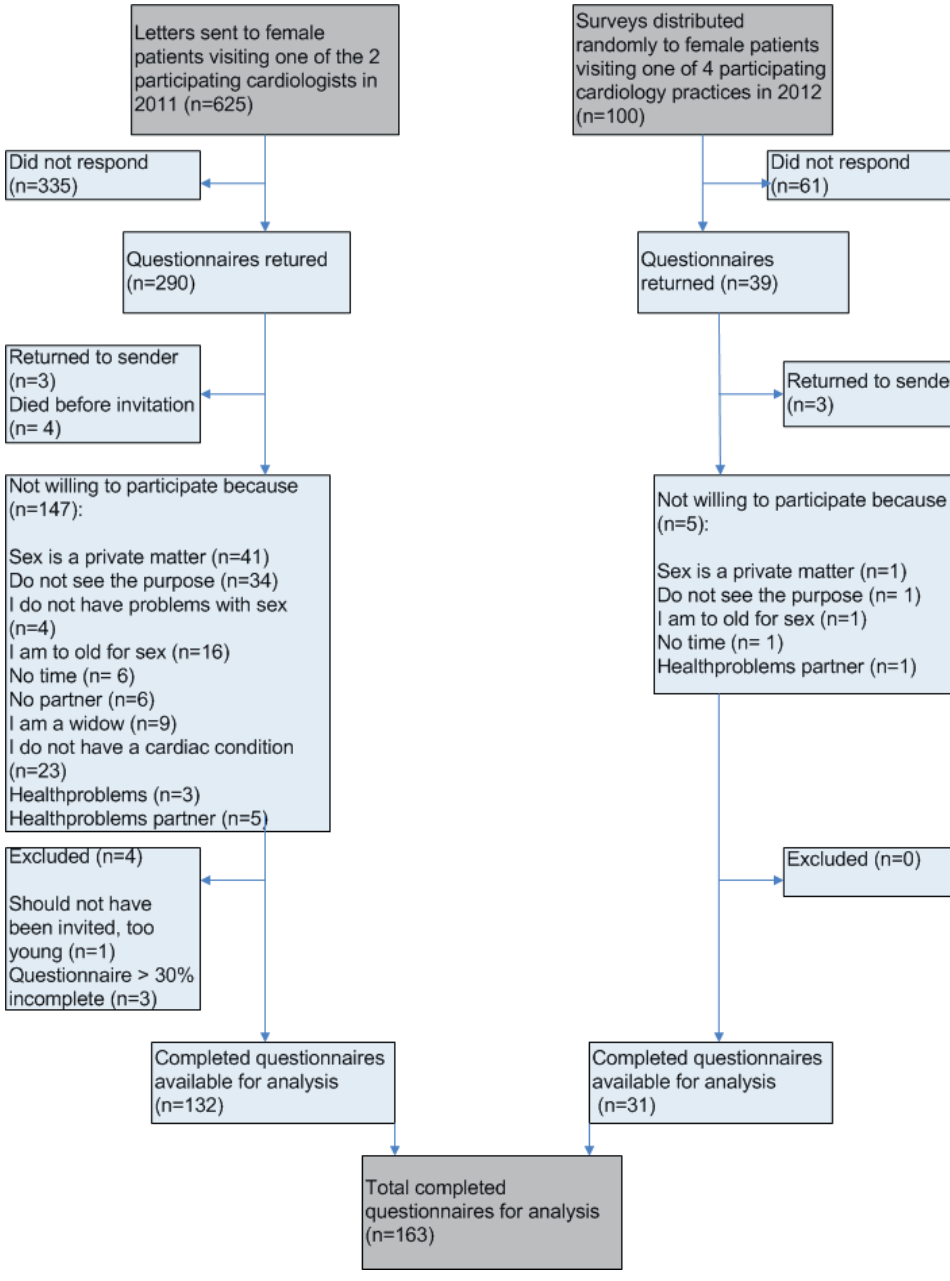
Setting and participants

In February 2013, a total of 625 surveys were mailed to a cross sectional cohort of adult female patients consulting one of the participating 'Cardiology Centers of the Netherlands' (CCN) (G.A.S, I.I.T., CCN location Amsterdam or G. J. d. G., CNN location Voorschoten) between January 2011 and January 2012. Furthermore 100 questionnaires were randomly distributed to adult female patients visiting the outpatient cardiology department of Leiden University Medical Center (academic hospital) or the Diaconessen Hospital Leiden (local general hospital) between May 2012 and January 2013. Questionnaires were distributed in a sealed envelope accompanied by a letter in which the nature, scope, objectives and contents of the questionnaire were explained and an information sheet explaining participation was voluntary and ensuring total anonymity. People unwilling to participate could mark the consent form stating their unwillingness; a question was added to obtain reason(s) not to participate. In the two other outpatient clinics, questionnaires were distributed by the secretary. Patients were invited to fill out the questionnaire at home and return it by mail in the provided freepost envelop. Questionnaires were processed by independent researchers (M.P.N and J.v.B.), and could not be traced back to individual patient records. The study was approved by the Committee for Medical Ethics (MEC) of Southwest Holland and the boards of the participating centers. The strictly anonymous design was the prerequisite; due to this design reminders could not been sent out to non-respondents.

Due to the cross-sectional study design, all women over 18 years consulting a cardiologist in one of the participating centers were considered eligible for participation. Patients visiting for routine checks or medical inspection were included in the study and data from both sexual active and sexual inactive women were obtained. Exclusion criteria were the inability to understand the Dutch or English language.

A study flow chart is displayed in Figure 1 indicating sources and methods of selection of participants.

Figure 1. Study flow diagram



Survey Instrument

Established, validated questionnaires about sexual function and quality of life were used to develop a 28-item gender-specific survey directed towards female patients with all possible indications for consulting a cardiologist. The survey consisted of three sections; in the first part demographic information was obtained, the second part was developed to explore prevalence of FSD, and the third part to gain insight into the needs of women with CVD regarding sexual health care in cardiology. Assessment of female sexual function was performed using the validated 6-item version of the Female Sexual Function Index (FSFI6), a frequently cited psychometric test for screening and diagnosis of FSD in clinical practice and research (13). The abbreviated version was used because it is an efficient instrument to disclose FSD, scoring for desire, arousal, lubrication, orgasm, satisfaction and pain (14). By keeping the questionnaire short, we aimed to reach a higher response rate and to avoid "straight line" (stereotypical) responding (15). Bother due to sexual dysfunction and its influence on the relationship was scored on a 0-10 scale, in which 0 meant no bother at all and 10 meant the most possible bother. Quality of the questionnaire was audited by a multidisciplinary expert panel with experience in the development of questionnaires.

Data Analysis

Results were summarized by reporting responses on all surveyed items. Frequencies of demographic characteristics, health behaviors, chronic conditions and aspects of sexual function were presented. Numerical demographic values were summarized as mean (SD). Prevalence of FSD was based on a FSFI6 cutoff score ≤19 (14). Differences in numerical data between demographic groups were analyzed with independent sample t-tests. χ^2 Tests were used to assess association between categorical respondents' characteristics and categorical responses. Bivariate correlations were used to correlate FSFI6- scores with bother-scores and linear regression analysis was used to identify predictors of an abnormal FSFI6 score. Statistical significance was defined as $p<0.05$, all tests were two-sided. Confidence intervals were defined as 95%. Analyses were conducted using SPSS release 20 (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic data

From the 725 women who received the questionnaire and consent form, 329 (45.4%) where returned. Of these respondents, 152 (46.2%) declined participation, 3 women had died (0.9%) and 7 (2.1%) questionnaires where returned to sender. A total of 167 women filled in the questionnaire, 3 were excluded because they where incomplete for more than 30%, 1 because the patient was under-aged, leaving 163 questionnaires for analysis (49.5%; see Figure 1).

Mean age of 163 respondents was 60.2 years (±13.7). For 74.8% of these women a cardiac diagnose was made, in the other 25.2% no cardiovascular problems were found.

No significant age differences were seen between women without a cardiac diagnosis (mean age 57.4 ±13.5, see Table 1) and those with CAD (p=0.243), hypertension (p=0.11) or arrhythmias (p=0.49).

However, women with heart failure, valvular disease or congenital heart disease were older than those without a cardiac diagnosis (mean ages 65.9±11.2, p=0.02; 70.6±11.8, p= 0.004 and 80.5±9.1, p=0.05 respectively).

Of those who did not use cardiovascular medication 39.3% (n=64), 51.6% were diagnosed with a cardiovascular problem. Cardiovascular agents were used by 60.7% of the respondents; 22.1% used one, 19.6% used two and 19.0% used three or more agents (Table 1).

Table 1. Characteristics of study sample

Patients Characteristics	n=163 [a]
Age, mean (range), years	60.2 (18-90)
Weight, mean (SD), kg	73.5 (±14.4)
Height, mean (SD), cm	167.0 (±10.5)
BMI mean, (SD), kg/m^3	27.0 (±12.0)
Nationality n (%)	
Dutch	147 (90.2)
Other western country	8 (4.9)
Non-western country	8 (4.9)
Cardiovascular agents[b], n (%)	
α-blocker	3(1.8)
ACE inhibitor	23 (14.0)
ARB	29 (17.7)
β-blocker	61 (39.0)

Table 1. Continued

Calcium-antagonists		24 (14.6)
Digoxin		2 (1.2)
Loop diuretic		18 (11.0)
Thiazide diuretic		5 (3.0)
Nitrates		7 (4.3)
Statins		34 (20.7)
Other		7 (4.3)
Co-medication[b] n (%)		
Coumarin derivatives		6 (3.7)
Platelet Aggregation Inhibitors		35 (1.6)
Diabetes medication		4 (2.4)
Anti-depressants/anti-psychotics		5 (3.0)
Smoking n (%)		
Yes		14 (8.5)
No		93 (56.7)
Quited < 1 year ago		4 (2.4)
Quited >1-5 years ago		11 (6.7)
Quited>5-10 years ago		12 (7.3)
Quited>10-20 years ago		12 (7.3)
Quited>20 years ago		18 (11.0)
Cardiac diagnose[b]	n (%)	Age, mean (range), years
Ischemic Heart Disease	21 (12.8)	63.0 (29-84)
Hypertension	54 (32.9)	64.8 (35-88)
Arrhythmias	59 (36.0)	58.0 (18-88)
Myocardial infarction	6 (3.7)	58.0 (29-82)
Heartfailure	2 (1.2)	66.5 (66-67)
Heart valve disease	23 (14.0)	67.2 (35-90)
Primary Myocardial Disease	2 (1.2)	63.0 (49-77)
Myxoom	2 (1.2)	52.0 (35-69)
Congenital Heart Disease	2 (1.2)	80.5 (74-87)
No cardiac diagnose	25 (15.2)	57.4 (28-77)

Abbreviations: *BMI,* Body mass index (m / l²); *ACE,* angiotensin-converting enzyme, *ARB,* Angiotensin receptor blocker

[a] Columns may not add to 164 due to missing value

[b] Multiple answers were possible, total exeeds 164

Female patients' perception: sexual healthcare in cardiology

To the question: "If the cardiologist would ask you about sexual problems during consultation, how would that make you feel?" on the one hand, 15% of respondents (n=163; multiple answers were possible) answered "uncomfortable", 5% "annoyed", 1% "offended" and 19% thought the cardiologist would not be able to help with sexual problems. On the other hand, 45% would not mind if the cardiologist asked about sexual function, 15% found it logical and almost 24% thought discussing sexual health was necessary for a complete consult.

Respondents' views about several possible options for improvements in sexual healthcare are displayed in Table 2.

Of the six women who had MI, none indicated attention for sexual health was necessary, three indicated not to have a sexual dysfunction, the other three indicated not to believe the cardiologist could help them with sexual problems. Of the heart failure patients (n=2) one felt too old for sex (age 67) and one said her condition was insufficient.

Women with sexual complaints

For women with self-indicated sexual dysfunction, an additional set of questions concerning experienced bother, treatment wish and preferred forms of treatment was posed, 35% of the women answered these questions.

Respondents were asked to score discomfort/bother experienced due to sexual complaints on a 0 to 10 scale. Mean bother score was 3.4 (±3.0), younger age was a predictor for higher bother scores (β=-0.09, SE±0.04; p=0.02). Mean influence of sexual dysfunction on marriage or relationship was 3.1 (±2.6) on a 0 to 10 scale and this was not correlated with age (r=-0.03, p=0.88).

Answers to the question: "Would you like treatment for your sexual problem(s)?" can be found in Table 2. Several reasons not to discuss sexual health with the cardiologist were mentioned; "these complaints are not related to my cardiac problem" was the most common (29%). "Sex is not important for me" (21%) and "I do not believe the cardiologist can help me with this kind of problems" (18%) were mentioned as well. Furthermore, 15% said to feel too old for sex (ages ranged from 60 to 74 years) and 9% answered that sexual function was a matter too intimate to discuss with the physician.

Table 2. Wish for treatment of sexual complaints and preferred forms of care as can be offered in the cardiology practice

Would you appreciate conversation with the cardiologist about possibilities to improve your sexual life?	**n=161 [a] n(%)**
Yes	9 (5.6)
No	70 (43.5)
Not applicable	82 (50.9)
Would you appreciate the option of discussing sexual issues during consultation with a specialized nurse?	**n=161[a]**
Yes	29 (18.0)
No	45 (28.0)
Not applicable	87 (54.0)
Would you like to receive written information about sexual dysfunction and its' possible solutions?	**n=161 [a]**
Yes	26 (16.2)
No	55 (34.2)
Not applicable	77 (47.8)
Would you like to be treated for your sexual problem/complaint(s)?	**n=56[b]**
Yes	3 (5.4)
Maybe	20 (35.7)
No	33 (58.9)
What would you like the cardiologist to do regarding your sexual complaints?	**n=23[c]**
Just listen to me	2 (8.7)
Give me some advise how to deal with it	3 (13.0)
Give me explanation about how it works	5 (21.7)
Refer me to a gynecologist	3 (13.0)
Refer me to a sexologist	2 (8.7)
Refer me to a pelvic floor physiotherapist	2 (8.7)
Give me information so I can read about it	22 (95.6)
Give me some information and let me think about treatment options at home	5 (21.7)

[a] Two respondents missed or skipped these questions

[b] Based on answers from 56 women; questions were only answers by women that indicate not to be satisfied with their sexual life

[c] Women that answered "yes" or "maybe" to the previous question.

[d] No significant differences were seen between women with different cardiovascular diagnoses regarding or between premenopausal (n=32) and postmenopausal women (n=131).

Specific groups and the demand for sexual healthcare

Female sexual dysfunction scored with the Female Sexual Function Index

FSD was defined as a Female Sexual Function Index-score (FSFI6) of 19 points or less. The FSFI6 was only validated for women who had been sexual active in the past four weeks, excluding all women that were not; the female sexual function index was scored for 104 women.

Prevalence of FSD was 61.5% (n=64/104), prevalence of FSD increased significantly with age (linear-by-linear association, p<0.001). As shown in Figures 2 and 3, increasing age had a strong negative correlation with FSFI6 score in the sexual active population (β=-0.18 (SE=0.04); p=<0.001). A higher age-related unstandardized coefficient was seen in women with hypertension (β=-0.35, SE±0.10; p=0.002), compared to normotensive women (β=-0.17, SE±0.05; p=0.001).

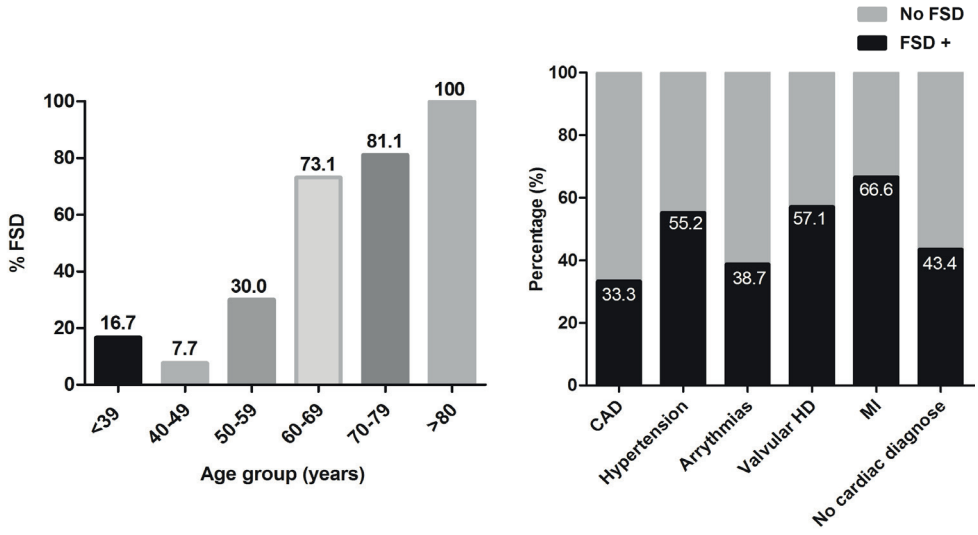
Low FSFI6 scores were not significantly associated with current and former smoking (p=0.436) or with BMI above 25 kg/m^3 (p=0.645). However, the hypertensive women (n=37) had significantly lower FSFI6 scores than normotensive women (mean scores 14.6 ±7.30 versus 17.3 ±5.62; p=0.04), a trend towards association with MI was seen (mean scores 10.0 ±8.73 versus 16.5 ±6.22; p=0.08) (see Figure 3).

Of those with FSD, 18% said to be very or moderately dissatisfied with their sexual life, 21% were equally satisfied as dissatisfied, and 61% said to be moderately or very satisfied. Women without FSD were satisfied more often than those with FSD (93% vs. 61%; p<0.001), unrelated to age. Influence of FSD that patients experienced on their marriage or relationship was correlated to the bother scored due to FSD (r=0.46, p=0.009). And difference was seen between women with- and without FSD (as measured with the FSFI6-score) regarding the wish for treatment of sexual complaints (yes or maybe) (linear-by-linear association, p=0.011).

Sexual inactive women

Fifty-seven women (35%) were sexual inactive in the past 12 month, these were significantly older than the sexually actives (mean age 68.5 ±11.6 compared to 55.8 ±12.6; p<0.001). The sexually inactive women were asked to state one or multiple reasons for this. The most common reason was the lack of a partner (divorced, single, widow) (41%). 24% answered 'Sex is not important for me', 29% accredited the sexual inactivity to physical problems and 24% said to be too tired. Thirty-five percent of the sexual inactive women (35%) indicated to have a sexual dysfunction, 18% of them indicated to be sexual inactive due this dysfunction, in 27% sexual (erectile) dysfunction of the partner was the reason. Differences between wishes regarding sexual healthcare in cardiology between sexual active and sexual inactive women can be found in Table 2.

Figure 2. Prevalence of female sexual dysfunction by age group and percentage of FSD by diagnose



Abbreviations: *CAD*, coronary artery disease, *Valvular HD*, valvular Heart Disease; MI= myocardial infarction; *FSD +* = female sexual dysfunction present
Based on data of 104 sexual active women.

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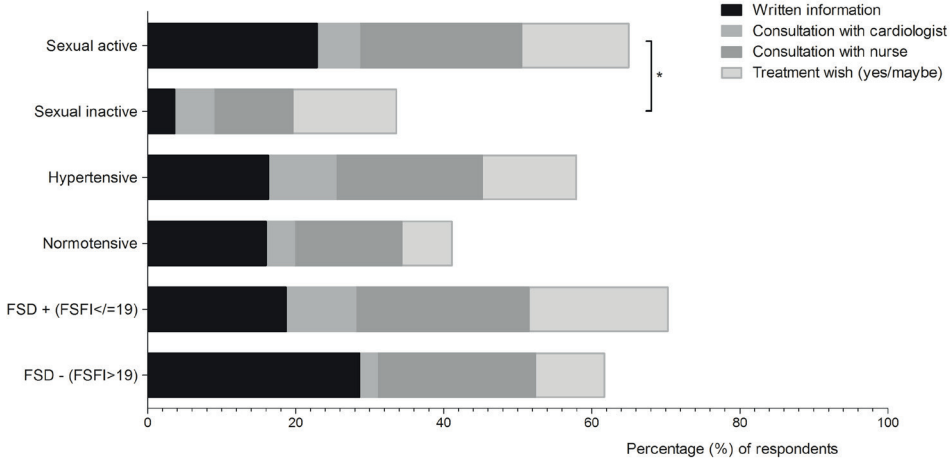
Figure 3. Preferred forms of sexual healthcare and wish for treatment



Based on answers of 163 women in different categories, not all women answered.
Totals: sexual active: n=104, sexual inactive: n=57, hypertensives: n=54, normotensives: n=106, FSD + (FSD present as measured with the FSFI): n= 64, FSD - (no FSD present when measured with the FSFI): n=40.

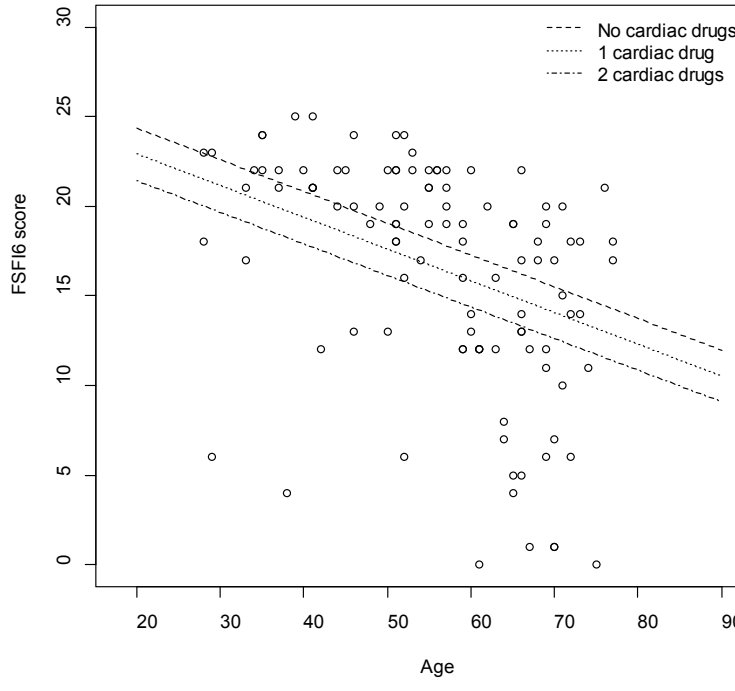
Medication

Using linear regression, number of cardiovascular agents was shown to be a predictor for lower FSFI6 scores (β= -1.47 (SE 4.31); p=0.001) per added agent, independent of age (Figure 4). Furthermore, the more cardiovascular agents used the more often a treatment wish was stated (linear-by-linear association, p=0.009).

A significant lower mean FSFI6 score was found in women using a β-blocker (14.0 ±6.2 versus 17.4 ±6.2; p=0.08) and in those using an ARB (12.2 ±7.9 versus 17.1 ±5.8; p=0.004). However, when corrected for age (β= -0.18 (SE 0.04); p<0.001) and number of agents used, the effects of both β-blockers and ARBs were not found predicting for FSD anymore (β=0.28 (SE 1.9); p=0.98 and β=-1.85 (SE 1.6); p=0.26 respectively), the number of agents the patient used however, remained predicting for low FSFI6 scores (β= -1.22 (SE 0.56); p=0.03). Nevertheless, women using β-blockers or ARBs indicated to be less satisfied with their sexual lives in general (linear-by-linear associations,

p= 0.019 and p=0.001 respectively) and less satisfied with their sexual relationship (linear-by-linear associations, p= 0.019 and p=0.014 respectively). This was not the case with the other antihypertensive agents. Women using a β-blocker wanted treatment for sexual dysfunction more often than those not using a β-blocker (linear-by-linear association; p<0.001), this was not observed in women using ARBs.

Figure 4. Female Sexual Function Index (FSFI6) score versus age and use of cardiovascular drugs.



DISCUSSION

Key findings of this study were: 1) 35% of women in our sample indicated sexual dysfunction was prevalent and 2) 40% of them would welcome treatment for it. Only a small minority would appreciate consultation about sexual health with the cardiologist. Consultation with a nurse and the availability of written information would be valued by 20%, unrelated to age. The necessity for sexual healthcare in cardiology was confirmed more often in women with FSD as scored with the Female Sexual Function Index. Higher percentages of sexual dysfunction were seen among hypertensive women and, the cumulative number of antihypertensive agents used was found to be negatively correlated with sexual function. To our knowledge, this was the first study evaluating the specific needs of a cross-sectional ambulant sample of women with CVD. The self-reported prevalence of sexual dysfunction was comparable to the rate found in the Observational Study Cohort of Women's Health Initiative among postmenopausal women with CVD (1). Measured with the FSFI6, more than 60% percent of sexual active women in our sample scored to have FSD, similarly in a sample of 2763 women with heart disease (mean age 67 years) a prevalence rate of 65% was found (2). The present study showed a higher rate of FSD in hypertensive women, confirming data of Doumas et al, who reported a higher prevalence of FSD in hypertensive- (42%) compared to normotensive women (19%)(3). The association between β-blocker use and sexual dissatisfaction was shown in several studies among women as well (3;16;17).

Antihypertensive combination therapy has been associated with higher rates of erectile dysfunction in men. Combination of a diuretic with a β-blocker, particularly the non-selective ones, increased the rate of sexual dysfunction and resulted in treatment discontinuation in men (18;19). However, until now, this has not been studied among women and has to be explored in future research.

Comparing results of this study with our previous study among men with CVD, the gender differences regarding sexuality are clear. Of 296 men visiting the cardiologist, 65% had erectile dysfunction (ED), sexual satisfaction and wish for treatment were significantly related to it. Compared to the women in present study, a significant higher proportion of men would appreciate consultation with the cardiologist (29.7% versus 5.4%) and 46% of men would appreciate consultation with a nurse to ask questions about sexual function, in contrast to 18% of women (20). In addition, whereas it is difficult to indicate if CVD has a direct effect on female sexual function (1;21); in men the link between ED and CVD is significant and has been shown and confirmed in many trials (10;22).

This study contributes to current, scarce, knowledge about FSD in women with CVD, indicating women have different needs than men with regards to sexual counseling.

Results have to be interpreted in the light of several limitations. We tried to minimize potential biases by providing detailed assurance and confidentiality and by pilot testing and refining our questionnaire. Still the relatively low response rate may have led to response bias. Moreover, the sensitive nature of the topic explored may have led to non-response bias. Especially singles, widows, and patients in poor mental or physical health may have decided not to participate. Epidemiologic literature showed non-respondents to have worse health status than the population average and to be less satisfied with medical care (23). Consequently, our results may be displaying an underestimation of FSD. Yet, distribution of demographic data in the sample and the obtained prevalence rates of FSD were consistent with those from prior population-based research among women with CVD (1;2;24). The majority of women with CVD are postmenopausal, likewise are most women in present study. While age is an important determinant in FSD, this age factor has to be taken into account while interpreting the data.

The fact that women, in comparison to men, attributed less importance to sexual function in general and related to their relationship, was to be expected and was already explained in the sixties by Masters and Johnson (25). Women's experience with sexual arousal is not focused on the physical responses, but is much more subjective and regulated by emotions and cognitions (26). Furthermore, aging women may devaluate their expectations regarding sex or its perceived importance (27). This may explain why only a relative small percentage of women with FSD would appreciate the various proposed options for improvement of sexual healthcare in cardiology. The subjective component of FSD makes it much more difficult to assess whether or not endothelial dysfunction in CVD has the same physical impact in female sexual function as it has in men. ED has been found to be a sentinel marker occurring years prior to cardiovascular events (28), but even if the same connection is found with female sexual function, the fact that FSD cannot objectively be measured implicates it will never be useful as marker for CVD in women.

For the cardiology practice, results of this study indicate sexual counseling does not have to be offered as actively in women as in men. In contrast to the recommendations made in the consensus document of the American Heart Association (12), our data point towards a passive approach with respect to sexual healthcare for women in the cardiology clinic. The availability of written material seems a good starting point, providing patients with information about sexual health in the context of CVD and lowering the threshold to initiate conversation about the subject. If a patient indicates sexual counseling is needed, the availability of a (specialized) nurse would be accommodating. This service would both be appreciated by the patient, and would reduce workload for the cardiologist.

In women with FSD using one cardiovascular agent, a switch in antihypertensive medication may significantly ameliorate sexual function. In several studies among males and in a few studies among female patients, the use of ARBs have been shown to leave sexual function unaffected (3;29;30) or even to improve sexual function (16;31;32). This however was not measured in multi-drug regimens. Our data indicated that the use of several antihypertensive agents together has a negative effect on female sexual function, independent of the combination used. This implicates that female sexual function would improve if the medication regiment would be emaciated. Studies regarding medication switches to improve sexual function in women have not yet been performed either. To provide recommendations for women who presenting with FSD while using antihypertensive agents, results of studies in men have to be extrapolated. Findings from observational and clinical studies pointed towards similar effects of antihypertensive drugs in male and female sexual function (17;32;33). Next to a switch to ARBs, if β-blocker use is necessary, a switch to the third-generation β-1 blocker Nebivolol may improve sexual function (34;35).

In case sexual dysfunction remains after diminishing and/or switching the medication, referral to a gynecologist or pelvic floor physiotherapist should be considered. For those in need for advice to improve their sexual life unrelated to physical problems, referral to a sexologist is preferred.

In conclusion, FSD is prevalent among women visiting the cardiology clinic, but in contrast to male sexual dysfunction (often ED) the burden appointed to it seems to be significantly smaller and only a minority of women indicate to appreciate conversation about sexual health with the cardiologist. The availability of written information about sexual function and/or the possibility of consultation with a specialized nurse may be good alternatives for patients with FSD.

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