Sex differences in selection of pacemakers: retrospective observational study

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Abstract

Objective: To evaluate the effect of patients' sex on selection of pacemakers.

Design: Retrospective univariate and multivariate analysis of a large database.

Setting: German central pacemaker register.

Subjects: Records collected at the register for 1992 and 1993 (n = 31 913), covering 64% of all implantations in Germany.

Main outcome measure: Probability of receiving a single chamber, dual chamber, or rate responsive pacemaker in relation to sex.

Results: Univariate analysis showed that women were more likely to receive single chamber pacemakers and less likely to receive dual chamber or rate responsive systems than men. After demographic and clinical variables were controlled for, women were still more likely to receive a single chamber system (atrial pacing: odds ratio 0.89, 95% confidence interval 0.74 to 1.07; ventricular pacing: 0.85, 0.80 to 0.92) and less likely to receive a dual chamber (1.20, 1.12 to 1.30) or a rate responsive system (1.26, 1.17 to 1.37) than men.

Conclusions: The data suggest sex differences in the selection of a pacemaker system which cannot be explained by the underlying cardiac disorder. Further research is needed to evaluate why guidelines for implanting pacemakers are not better adhered to.

Introduction

Pacemakers are the standard treatment for symptomatic bradyarrhythmia. Professional societies have issued guidelines for the implantation of cardiac pacemakers.[1–3] Although these guidelines have all been similar, considerable differences have been reported in the frequency of implantation of pacemakers and in the system selected.[4] Relatively little is known about the reasons for these differences.[5] There is some evidence that patients' sex might play a part in clinical decision making.[6–8] We used a large database to analyse whether sex can explain differences in the selection of pacemaker systems.

Subjects and methods

Doctors who perform implants transfer information available from the European pacemaker patient identification card to the German central pacemaker register on a voluntary basis. Customs' statistics and manufacturers' sales figures suggest that the register comprises 64% of all implantations in Germany. Of the 880 German hospitals in which implants are done (number estimated by a survey), 634 (72%) sent their reports to the register.[9] Our analysis is based on complete data for the years 1992 and 1993. We excluded cases that had classification errors (for example, non-existent categories) from the total of 15 914 patients in 1992 and 15 999 patients in 1993. Table 1 gives the characteristics of the patients.

Statistical analysis

We examined the pooled data for 1992 and 1993 according to patient characteristics (age, sex, clinical symptoms, underlying disease, electrocardiographic findings), type of pacemaker (single chamber, dual chamber), and rate responsive systems. The χ^2 test was used to analyse discrete variables and Student's t test used for continuous variables.

For logistic regression we defined the type of pacemaker as the dependent variable and age, sex, clinical symptoms, underlying disease, and electrocardiographic findings as independent variables. Explanatory variables for the selection of a specific pacemaker were first determined in a univariate logistic regression. We then used a multivariate model adjusting for age, clinical symptoms, underlying disease, and electrocardiographic findings to determine the effect of sex on choice of pacemaker. Cases with more than one missing value were excluded from univariate regression, and only complete datasets were used in the multivariate regression. All data were processed with SAS 6.08 software. A P value < 0.05 was considered significant. All tests were two tailed.

Results

Table 1 shows that single chamber systems were implanted in a higher proportion of women (atrial 492 (3.2%), ventricular 11 065 (71.9%)) than men (atrial 429 (2.7%), ventricular 10 499 (66.1%)). In contrast, men received more dual chamber (4892 (30.8%)) and rate responsive systems (4273 (26.9%)) than women (3770 (24.5%), 3186 (20.7%)). Sex differences were also found for various clinical variables.

In the univariate analysis, where 21 858 patients could be included (68.5% of the sample), age, sex, several clinical symptoms, underlying disease, and electrocardiographic findings were significantly associated with the pacemaker system selected for implantation (table 2). After the effects of age, clinical symptoms, underlying disease, and electrocardiographic findings had been adjusted for in a multivariate analysis (n = 16 289 (51.0% of the data)), women were still more likely to receive a ventricular single chamber pacemaker and less likely to receive a dual chamber or rate responsive system than men (table 3).

Discussion

Analysis of data from over 15 000 patients suggests a sex bias in choice of a pacemaker system. Women were more likely to receive single chamber systems and less likely to receive dual chamber or rate responsive systems than men. Can these findings be explained by differences in the underlying cardiac disorders or demographic data? In our cohort a higher proportion of men presented with an atrioventricular block than women. It is generally accepted that dual chamber pacemakers achieve better haemodynamic results than

Table 1 Characteristics of patients receiving pacemaker by sex*

	Men			Women			
	No (%)	Mean age	Median age	No (%)	Mean age	Median age	P value†
Age (years)		n=15 648			n=15 110		
Mean (SD)		73.8 (12.1)			77.6 (10.9)		<0.001
Median (interquartile range)			73.6 (65.8-80.8)			77.4 (70.4-82.4)	
Type of pacemaker		n=15 884			n=15 389		
Single chamber atrial	429 (2.7)	67.5	68.3	492 (3.2)	70.9	72.8	<0.005
Single chamber ventricular	10 499 (66.1)	73.2	76.4	11 065 (71.9)	75.8	78.7	<0.001
Dual chamber	4892 (30.8)	67.7	70.1	3770 (24.5)	69.8	72.4	<0.001
Rate responsive‡	4273 (26.9)	68.1	70.5	3186 (20.7)	70.0	72.8	<0.001
Symptoms		n=12 005			n=11859		
Syncope	4154 (34.6)	71.8	74.5	4554 (38.4)	75.4	78.3	<0.001
Dizziness	3229 (26.9)	72.1	73.7	3368 (28.4)	74.3	77.0	<0.01
Bradycardia	2389 (19.9)	71.8	73.3	2063 (17.4)	73.9	77.3	<0.001
Heart failure	708 (5.9)	73.1	76.2	629 (5.3)	75.8	78.7	<0.05
Electrocardiographic result		n=11 874			n=11 788		
Atrioventricular block	4346 (36.6)	71.5	74.0	3902 (33.1)	74.1	78.0	<0.001
Sick sinus syndrome	3930 (33.1)	72.0	73.7	4644 (39.4)	74.8	77.2	<0.001
Atrial fibrillation/flutter	2209 (18.6)	73.4	75.8	2181 (18.5)	76.1	78.7	0.814
Aetiology		n=1 397			n=11 263		
Ischaemic	3932 (34.5)	73.7	75.5	3627 (32.2)	76.1	78.5	<0.001
Fibrosis	878 (7.7)	71.7	73.8	969 (8.6)	74.9	77.5	<0.01
Carotid sinus syndrome	524 (4.6)	71.0	72.4	338 (3.0)	75.9	78.3	<0.001

*Categories with small numbers and cases labelled unknown are not included in the table. †Age analysed by t test, all other variables by χ^2 test. ‡Percentage of the above pacemaker systems with rate responsive function.

Table 2 Univariate analysis of variables determining selection of pacemaker in 21 858 patients*

	Type of pacemaker (odds ratio (95% CI))			
	Single chamber atrial	Single chamber ventricular	Dual chamber	Rate responsive
Age	0.84 (0.80 to 0.88)	1.35 (1.33 to 1.39)	0.75 (0.70 to 0.80)	0.80 (0.78 to 0.82)
Sex	0.84 (0.71 to 0.98)	0.76 (0.72 to 0.81)	1.38 (1.30 to 1.47)	1.38 (1.29 to 1.47)
Symptoms:				
Syncope	1.04 (0.87 to 1.21)	1.15 (1.08 to 1.23)	0.85 (0.79 to 0.91)	0.65 (0.60 to 0.69)
Dizziness	1.64 (1.39 to 1.90)	0.78 (0.73 to 0.83)	1.20 (1.13 to 1.29)	1.19 (1.10 to 1.27)
Bradycardia	0.74 (0.58 to 0.91)	1.11 (1.03 to 1.20)	0.93 (0.85 to 1.01)	1.09 (1.00 to 1.18)
Heart failure	0.15 (0.07 to 0.25)	1.09 (0.95 to 1.23)	1.03 (0.90 to 1.18)	1.54 (1.35 to 1.75)
Electrocardiographic results:				
Atrioventricular block	0.06 (0.04 to 0.09)†	0.35 (0.32 to 0.38)	3.85 (3.57 to 4.16)	0.93 (0.87 to 1.01)
Sick sinus syndrome	13.29 (11.11 to 15.42)	0.89 (0.84 to 0.94)	0.80 (0.75 to 0.85)	1.19 (1.12 to 1.27)
Atrial fibrillation/flutter	0.11 (0.07 to 0.17)†	14.28 (12.48 to 16.08)	0.06 (0.05 to 0.07)‡	1.01 (0.92 to 1.08)
Aetiology:				
Ischaemic	0.71 (0.59 to 0.83)	1.43 (1.33 to 1.52)	0.71 (0.66 to 0.77)	0.68 (0.63 to 0.74)
Fibrosis	0.03 (0.02 to 0.04)	0.81 (0.73 to 0.90)	1.28 (1.15 to 1.43)	1.04 (0.93 to 1.16)
Carotid sinus syndrome	0.59 (0.35 to 0.88)	2.63 (2.13 to 3.17)	0.37 (0.30 to 0.45)	0.34 (0.27 to 0.43)

*Categories used in logistic regression were age: older patients/younger patients (10 year intervals); sex: men/women; and symptoms, electrocardiography, and aetiology: yes/no. †n<25. ‡n=119—cases with rare indications, low degree of disorder (atrioventricular block), or intermittent disorder.

single chamber systems in atrioventricular block.[2 10] Women, on the other hand, had a higher frequency of sinus node dysfunction. In this disorder a single chamber system often seems to be sufficient, although several authors have found that dual chamber pacemakers produce better outcomes in terms of haemodynamics, subjective symptoms, the development of atrial fibrillation, and prognosis.[11] Finally, cardiovascular diseases occur at a later age in women than in men.[12] In our cohort women were on average 3.8 years older than men. Doctors generally implant single chamber pacemakers in elderly patients rather than dual chamber systems.[13]

Several studies of factors influencing cardiovascular interventions showed that sex was no longer a determinant once demographic and clinical variables had been adjusted for.[14 15] In our study, however, even after we controlled for demographic and various clinical variables sex remained independently associated

with the selection of a pacemaker system. Our results agree with two retrospective studies in the United States in which women were found to receive a dual chamber system less frequently than men.[16 17] The clinical importance of the suggested undertreatment of women with dual chamber and rate responsive pacemakers is not easy to evaluate. In addition to the

Table 3 Variables determining selection of pacemaker in multivariate logistic regression on 16 289 patients*

	No (%) receiving treatment		Multivariate adjusted
Type of pacemaker	Men	Women	odds ratio* (95% CI)
Single chamber atrial	2226 (2.8)	260 (3.2)	0.89 (0.74 to 1.07)
Single chamber ventricular	5680 (69.6)	6069 (74.6)	0.85 (0.80 to 0.92)
Dual chamber	2252 (27.6)	1802 (22.1)	1.20 (1.12 to 1.30)
Rate responsive†	1852 (22.7)	1482 (18.2)	1.26 (1.17 to 1.37)

*Adjusted for age, electrocardiographic results, symptoms, and aetiology; the ratios are men/women.
† Number of above pacemaker systems with rate responsive function.

Key messages

- Use of pacemakers varies despite guidelines, and the reasons for this are unclear

- In this study women were more likely to receive single chamber pacemakers and less likely to receive dual chamber and rate responsive pacemakers than men

- Demographic and clinical variables cannot fully explain these differences

- Prospective studies are needed to evaluate the effect of sex and other non-medical variables on the selection of pacemakers

advantages of dual chamber pacemakers in patients with atrioventricular block and sinus node dysfunction mentioned above, rate responsive systems have been shown to offer haemodynamic advantages over fixed rate systems in patients with chronotropic incompetence receiving ventricular single chamber pacing or dual chamber pacing.[18] Although there is evidence that patients treated by advanced pacing have a better quality of life,[19] it is not known whether this improvement is equal in men and women.

Is there sex discrimination?

What other reasons could there be for doctors deciding in favour of a single chamber pacemaker in women? Firstly, there are some "soft" indications for implanting pacemakers (class II indications in the American College of Cardiology/American Heart Association guidelines[2] and corresponding recommendations in many countries, including Germany) Furthermore, guidelines are not always unanimously adhered to in clinical practice.[5 20] Doctors are known to behave differently towards men and women as far as both diagnostic and therapeutic strategies are concerned.[21] Doctors seeing women with "soft" indications may tend to implant single chamber pacemakers whereas they choose dual chamber for men. Some of the "hard" indications may also be being neglected in women. Women often present their symptoms differently from men.[22] They are more likely to receive the same treatment as men if they present their symptoms as men do.[23] Finally, we found some published evidence that women sometimes reject sophisticated care in favour of more simple treatments. They may therefore choose not to have dual chamber systems.[24]

The database we used represents two thirds of the implantations performed in Germany. Since the percentage of reporting hospitals slightly exceeds the percentage of reported implantations, hospitals with a lower frequency of implantations may be overrepresented. However, for this majority of hospitals (72%) sex differences were present in selection of pacemakers. Sex was an independent determinant of choice of pacemaker, with women receiving roughly 20% fewer rate responsive and dual chamber systems then men. Missing data meant that we could include only 16 289 of the 31 913 records in the multivariate logistic regression analysis, and we could not control our data for variables such as left ventricular function, intermittent dysrhythmia, or multimorbidity that might have contributed to the differences found. In addition, our results do not necessarily apply to other countries. However, a similar sex bias has been shown to be likely

in the United States at least.[16 17] Study limitations and the retrospective design of our analysis do not allow a definite explanation for the sex bias. Prospective studies that include clinical endpoints such as survival or quality of life are needed to investigate this difference in more detail and reveal its potential implications.

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Science commentary: Pacemakers

Cardiac pacing began in the 1950s with the aim of preventing symptomatic bradycardia. Single chamber pacemakers, in which one lead is introduced into the ventricle, achieve this but they cannot increase the heart rate when people take exercise. They also fail to ensure that the atria and ventricles contract in synchrony.

Modern pacemakers now include dual chamber and "rate responsive" devices. With dual chamber pacemakers, leads enter the right atrium and ventricle, allowing both atrium and ventricle to be paced and sensed. If the sinus node is working dual chamber pacing enables atrial activity to be tracked by the ventricle. If the sinus node is diseased extrinsic sensors can supply additional information to decide an appropriate pacing rate. This means that when patient demand goes up, the pacemaker responds accordingly.

For example, some pacemakers contain a piezo-electric crystal to detect motion. When the crystal vibrates—in response to body activity—it produces a tiny voltage which feeds into the circuit, triggering an increase in pacing rate. Other sensors detect the release of catecholamines due to exercise or emotion. Catecholamines shorten the QT interval on the electrocardiograph, which can be monitored easily by the device. Other sensors can detect respiratory rate and acceleration.

Many devices also include safety features to avoid inappropriate rate rises. Some rely on a number of sensors as a cross checking mechanism. These can detect the difference between false positive movements caused, for example, by external motion around a person sitting in a train and true movements caused by walking or running.

Other pacemakers include mode switching devices which are designed to detect atrial arrhythmias. These can distinguish the onset of paroxysmal atrial fibrillation from the sudden onset of exercise and will reset the ventricular rate to a non-tracking mode of 70 beats per minute during the period of the arrhythmia.

The average age of patients receiving pacemakers in Britain is 73. Younger patients are likely to get more sophisticated devices. Several multicentre trials have been set up to establish the best policy, including the UKPACE trial which will assess the clinical impact and the cost utility (the value of quality of life benefits) of dual chamber pacing in elderly patients with heart block.

Abi Berger, *science editor, BMJ*

Rapid resolution of symptoms and signs of intracerebral haemorrhage: case reports

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Although intracerebral haemorrhage causes prolonged or permanent focal neurological dysfunction, neurological deficits[1] and lesions[2] may sometimes resolve within a few days. To my knowledge no one has reported resolution of the symptoms and signs of intracerebral haemorrhage within 24 hours, although the possibility has been recognised.[3] Intracerebral haemorrhage is therefore not considered to be a cause of transient focal neurological attacks and is not included in the differential diagnosis of transient ischaemic attacks.[4] Clinicians tend to diagnose transient ischaemic attacks on symptoms alone and to start antiplatelet drug treatment pending the results of computed tomography. This is particularly the case in developing countries where computed tomography is scarce. I report two cases of intracerebral haemorrhage in which the focal neurological symptoms and signs resolved within 24 hours.

Case reports

Case 1—A 58 year old woman awoke one night with a numbness and weakness of her left arm and leg. By the morning these had slightly improved. Her doctor diagnosed a transient ischaemic attack. She started aspirin treatment and was advised to see a specialist. By evening she was admitted to hospital. On examination her symptoms had resolved completely and she did not have weakness or sensory impairment. A computed tomogram showed a small intracerebral haemorrhage in the region of the putamen (figure a).

Case 2—A 65 year old man was admitted 2 hours after he had developed a headache, weakness of the left arm and leg, deviation of the mouth, and slurring of speech. He had a history of hypertension and had been drinking alcohol excessively during the 2 weeks before admission. His blood pressure was 190/100 mm Hg—he had recently stopped taking antihypertensive drugs. He had a mild facial weakness and weakness of the left arm and leg. He was unable to use his left hand to button his shirt, and he dragged his leg when walking. He did not have sensory impairment or a hemianopia. A computed tomogram showed a small intracerebral haemorrhage in the region of the putamen (figure b). The next morning he was symptom free and did not have any weakness on testing.

Comment

The possibility that symptoms and signs of small intracerebral haemorrhages can resolve within 24

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