

## Effects of Sex on the Incidence of Cardiac Tamponade After Catheter Ablation of Atrial Fibrillation: Results From a Worldwide Survey in 34 943 Atrial Fibrillation Ablation Procedures

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## Effects of Sex on the Incidence of Cardiac Tamponade After Catheter Ablation of Atrial Fibrillation Results From a Worldwide Survey in 34 943 Atrial Fibrillation Ablation Procedures

Yoav Michowitz, MD; Michael Rahkovich, MD; Hakan Oral, MD; Erica S. Zado, PA-C; Roland Tilz, MD; Silke John, MD; Arnaud Denis, MD; Luigi Di Biase, MD; Roger A. Winkle, MD; Evgeny N. Mikhaylov, MD, PhD; Jeremy N. Ruskin, MD; Yan Yao, MD; Mark E. Josephson, MD; Hildegard Tanner, MD; John M. Miller, MD; Jean Champagne, MD; Paolo Della Bella, MD; Koichiro Kumagai, MD; Pascal Defaye, MD; David Luria, MD; Dmitry S. Lebedev, MD, PhD; Andrea Natale, MD; Pierre Jais, MD; Gerhard Hindricks, MD; Karl-Heinz Kuck, MD; Francis E. Marchlinski, MD; Fred Morady, MD; Bernard Belhassen, MD

**Background**—Cardiac tamponade is the most dramatic complication observed during atrial fibrillation (AF) ablation and the leading cause of procedure-related mortality. Female sex is a known risk factor for complications during AF ablation; however, it is unknown whether women have a higher risk of tamponade.

**Methods and Results**—A systematic Medline search was used to locate academic electrophysiological centers that reported cases of tamponade occurring during AF ablation. Centers were asked to provide information on cases of acute tamponade according to sex and their mode of management including any case of related mortality. Nineteen electrophysiological centers provided information on 34 943 ablation procedures involving 25 261 (72%) men. Overall, 289 (0.9%) cases of tamponade were reported: 120 (1.24%) in women and 169 (0.67%) in men (odds ratio, 1.83;  $P < 0.001$ ). There was a reciprocal association between center volume and the occurrence of tamponade with substantially lower risk in high-volume centers. Most cases of tamponade occurred during catheter manipulation or ablation; women tended to develop more tamponades during transseptal catheterization. No sex difference in the mode of management was observed. However, 16% cases of tamponade required surgery with lower rates in high-volume centers. Three cases of tamponade (1%) culminated in death.

**Conclusions**—Tamponade during AF ablation procedures is relatively rare. Women have an  $\approx 2$ -fold higher risk for developing this complication. The risk of tamponade among women decreases substantially in high-volume centers. Surgical backup and acute management skills for treating tamponade are important in centers performing AF ablation. (*Circ Arrhythm Electrophysiol.* 2014;7:274-280.)

**Key Words:** atrial fibrillation ■ cardiac tamponade ■ catheter ablation ■ sex

Catheter ablation of atrial fibrillation (AF) is one of the most complex interventional procedures in cardiology. The procedure has been associated with a minimal but nevertheless important risk of major complications.<sup>1-5</sup> Cardiac tamponade is the most frequently encountered procedure-related complication occurring in 1.2% to 1.3% of patients in 2 worldwide surveys<sup>2,6</sup> and 1.3% in a European survey.<sup>7</sup> It is also the main cause of procedure-related mortality, responsible for 25% of lethal cases.<sup>8,9</sup>

**Editorial see p 195**  
**Clinical Perspective on p 280**

Female sex is a known risk factor for complications during AF ablation.<sup>1,3,4,10</sup> In a study of 40 patients who developed cardiac tamponade during AF ablation at 3 institutions,<sup>11</sup> half of the patients were women, despite the known lower prevalence of women undergoing AF ablation.<sup>12</sup> In contrast in a series of 3265 patients (16% women) undergoing AF ablation, women did not experience more tamponade.<sup>10</sup> Higher cardiac perforation risk was also observed in women undergoing percutaneous coronary interventions,<sup>13</sup> devices implantations,<sup>14</sup> and catheter ablation of accessory pathways.<sup>15</sup>

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The purpose of the present study was to evaluate the relationship between patient sex and cardiac tamponade in a large patient cohort undergoing catheter ablation of AF.

## Methods

### Data Source and Center Selection

A Medline search was used to locate academic electrophysiological centers that are involved in AF ablation. The systematic Medline review was conducted by 2 investigators with the typed search words atrial fibrillation ablation. The search was limited to English language articles published between 2000 and 2012 that involved only patients aged >19 years. All centers with publications reporting tamponade as a procedure complication were eligible for inclusion.

Meta-analyses, multicenter trials, and case reports were excluded, as well as publications that involved patients with AF with associated cardiomyopathies, valvular heart disease, or uncommon cardiac anatomy or those who underwent surgical ablation of AF. Studies that involved the use of Hansen or Stereotaxis for catheter manipulation or high-intensity focused ultrasound as the source of energy were also excluded.

### Data Acquisition

All electrophysiological center directors were contacted and asked to provide detailed information on (1) the total number of AF ablation procedures performed in their laboratory; (2) the total number of procedures performed in patients of each sex; (3) the total number of acute tamponade occurring during or within 24 hours after the procedure in regard to patient sex; (4) the age of patients experiencing tamponade; (5) the mode of management of tamponade (pericardiocentesis, surgery, or both); and (6) any case of 30-day mortality that was assumed to result from tamponade.

The cooperating centers were also asked about (1) the use of intracardiac echocardiography (ICE) or transesophageal echocardiography for transseptal puncture and monitoring pericardial space; (2) the average power settings during AF ablation they used; and (3) the mode occurrence of tamponade according to patient sex: during transseptal puncture, catheter manipulation, or ablation in the left atrium. The study was approved by the Tel-Aviv Medical Center institutional review committee.

### Statistical Analysis

All data were summarized as number and percent in each center. The calculation of the combined effect size was done as a meta-analysis. At the first step, a heterogeneity test was done, followed by the calculation of the fixed and random combined effect size using DerSimonian and Laird method,<sup>16</sup> and the results were displayed as a forest plot.

The estimation of the association between the center experience and the percent of tamponade was done using regression curve estimation for inverse association ( $y=a+bx$ ). We assumed that the responses from centers were representative and that nonresponse bias was negligible. All analyses were considered significant at  $P<0.05$  (2-sided). Categorical data were analyzed using the  $\chi^2$  test. The Comprehensive Meta-analysis software was used for the meta-analysis (<http://www.meta-analysis.com/index.php>), whereas all other analyses were performed using the SPSS software version 21.0 (2012).

## Results

### Medline Search

The search permitted retrieval of 2740 citations. After reviewing all abstracts and when necessary the full articles we identified 136 reports from 85 electrophysiological centers that were compatible with the inclusion criteria.

Overall 19 centers provided details of their entire AF ablation patient cohort, whereas 2 (#16 and #17) that provided a large number of patients only gave data on selective consecutive years (Table 1). Ten centers provided data on the occurrence of

tamponade in the study group described in their published report but not in their entire AF ablation cohort. Therefore, these centers were not included in the present study. In 6 instances the corresponding authors could not be located. Authors from 3 centers responded but could not provide the requested data. Forty-seven electrophysiological centers did not answer our e-mails.

### Study Patient Cohort

Overall, 34 943 AF ablation procedures were conducted in the 19 participating centers: 25 261 (72%) in men and 9682 (28%) in women. There were 289 (0.84%) cases of acute tamponade of which 169 (0.67%) occurred in men and 120 (1.24%) in women ( $P<0.0001$ ). The distribution of procedures and tamponade among the various centers is provided in Table 1, with  $Q$  value of 17.3 in the heterogeneity test ( $P=0.50$ ). The average age of men with tamponade was  $62\pm 9$  years (range, 32–83 years; median, 62) was comparable with that of women,  $63\pm 9$  years (range, 21–82 years; median 64;  $P=0.16$ ).

An odds ratio plot is provided in Figure 1, demonstrating an overall 83% higher risk (odds of 1.83) for women to develop tamponade during AF ablation. Individually in 17 of 19 centers there was a higher proportion of women who experienced tamponade; however, the sex difference reached statistical significance ( $P<0.05$ ) in only 5 centers.

### Analysis According to Center Procedural Volume

A regression curve demonstrating the relationship between center volume and tamponade percentage is provided in Figure 2. A reciprocal relationship forces the curve to flatten out >1500 with an asymptotic value of 0.45%. Analyzing men and women separately (Figure 3) shows similar regression lines. In men, the incidence of tamponade decreases from 0.73% (for 1000 patients) to 0.45% (for  $n=\infty$  patients), whereas in women the incidence of tamponade decreases from 0.87% (for 1000 patients) to 0.5% (for  $n=\infty$  patients).

### Procedural Characteristics Related to Tamponade

Eighteen of 19 (95%) centers provided detailed information about procedural characteristics related to tamponade in 279 patients. The use of ICE or transesophageal echocardiography for transseptal puncture and monitoring pericardial space was systematic in 6 electrophysiological centers (#6, 9, 11, 13, 14, and 18), whereas it was not used in 9 (2–5, 8, 10, 15–17). Center #7 used ICE in the vast majority of cases but in none of the tamponade cases. Center #19 used ICE in >60% of cases, whereas the remaining centers started to use ICE/transesophageal echocardiography routinely only recently (#1) or as needed (#12). Power settings were not significantly different between centers, ranging from 20 to 35 W in the posterior wall and  $\leq 40$  W elsewhere. Lesion duration varied from 15 to 60 seconds and temperature <42 to 45°C. Center #13 used 50 W during ablation, however, with continuous movement. Center #3 also used cryoballoon. Ten cases of tamponade were related to discernible steam pops (1 center reported the occurrence of steam pops without the development of tamponade). Forty-three tamponades (27 men [16.5%], 16 women [13.7%];  $P=0.6$ ) were diagnosed post procedurally.

Of a total of 279 tamponades (116 women) reported in the 18 electrophysiological centers, presumed mechanism

**Table 1. Study Patient Cohort and Incidence of Cardiac Tamponade Among the Participating Centers**

Institution	Total No. of Procedures	Total No. of Tamponades	Tamponades, %	Total No. of Procedures in Men	Total No. of Procedures in Women	Tamponade in Men		Tamponade in Women	
						No.	%	No.	%
1	264	6	2.27	183	81	1	0.55	5	6.17
2	264	11	4.17	187	77	7	3.74	4	5.19
3	429	7	1.63	334	95	4	1.20	3	3.16
4	857	6	0.70	637	220	4	0.63	2	0.91
5	893	12	1.34	641	252	10	1.56	2	0.79
6	990	8	0.81	841	149	4	0.48	4	2.68
7	1020	20	1.96	616	404	6	0.97	14	3.47
8	1067	10	0.94	818	249	6	0.73	4	1.61
9	1117	21	1.88	809	308	10	1.24	11	3.57
10	1267	15	1.18	876	391	8	0.91	7	1.79
11	1376	10	0.73	975	401	6	0.62	4	1.00
12	1432	15	1.05	808	624	4	0.50	11	1.76
13	1504	9	0.60	1083	421	5	0.46	4	0.95
14	2751	6	0.22	1946	805	4	0.21	2	0.25
15	2923	19	0.65	2349	574	14	0.60	5	0.87
16	3356	24	0.72	2210	1146	13	0.50	11	1.13
17	3498	24	0.69	2344	1154	14	0.60	10	0.87
18	4259	24	0.56	3315	944	19	0.57	5	0.53
19	5676	42	0.74	4289	1387	30	0.70	12	0.87
Total	34 943	289	0.83	25 261	9682	169	0.67	120	1.24

of tamponade was related to radiofrequency energy delivery in the left atrium, unknown, catheter manipulation, or transseptal puncture in 33.3%, 32.9%, 22.9%, and 10.8% patients, respectively (Table I in the Data Supplement). Women tended to develop more tamponades during transseptal catheterization (16.3% versus 6.7%;  $P=0.046$ ).

### Mode of Tamponade Management

Of the 289 cases of tamponade reported by the 19 participating centers, 243 (84%) were treated by pericardiocentesis only, 43 (15%) by pericardiocentesis followed by surgery, and 3 (1%) by surgery-only (Table 2). All 3 patients treated by surgery-only were women. There was no sex difference in the percentage of patients managed by surgery ( $P=0.125$ ). There was an inverse correlation between the proportions of patients with tamponade treated by surgery and the center procedural volume ( $r=-0.466$ ;  $R^2=0.217$ ;  $P=0.044$ ; Figure 4).

### Tamponade-Related Mortality

There were 3 death events (1%) among the 289 cases of cardiac tamponade. Mortality rate resulting from tamponade was 0.008% for all procedures. The 3 lethal cases occurred in different centers and involved men only. One case of tamponade was identified several hours after the procedure with no evidence of pericardial effusion on ICE at the end of the procedure. The other 2 were diagnosed in the electrophysiological laboratory. All tamponade-related deaths occurred a few days after the procedure.

## Discussion

### Main Findings

To the best of our knowledge this is the largest study evaluating sex difference in the risk of tamponade during AF ablation. The occurrence of tamponade during AF ablation procedures was found to be relatively rare (0.84%); however, women had an 83% higher risk for developing this complication. The risk of developing tamponade was inversely related to center volume with a substantial decrease in women risk in high-volume centers. Surgical management was required in 16% of cases of tamponade irrespective of patient sex, whereas 1% of cases of tamponade resulted in death.

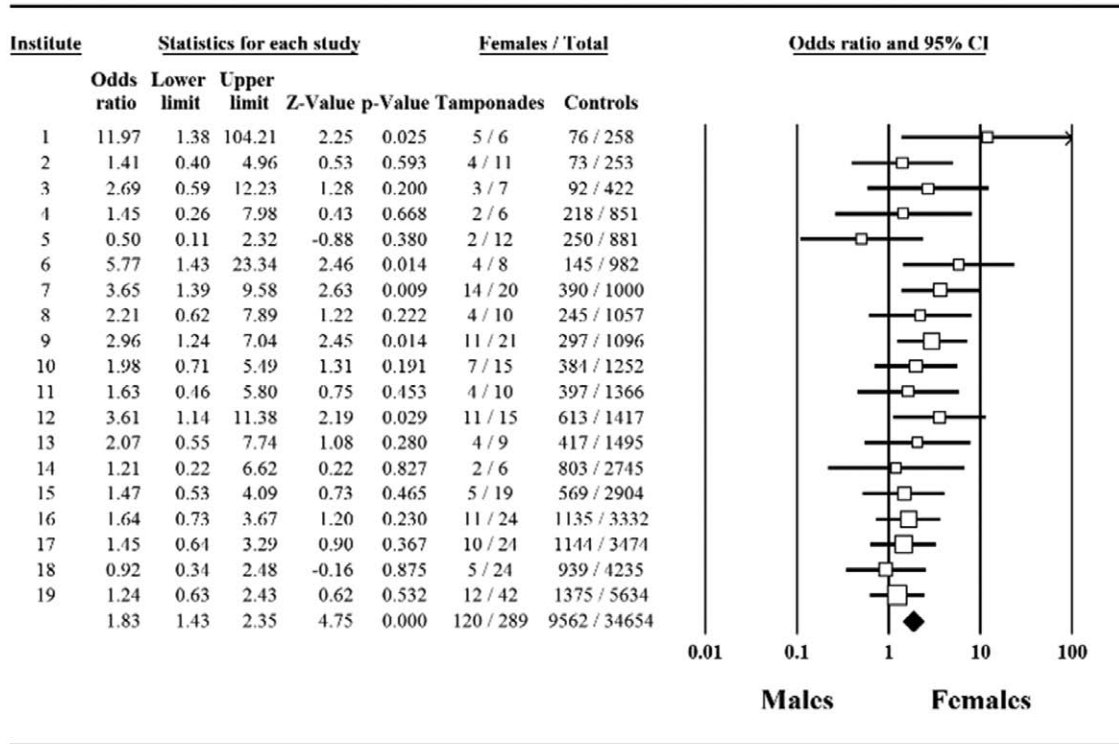
### Sex and Risk of Tamponade

Patel et al<sup>10</sup> examined 3265 patients who underwent AF ablation, of whom 518 (16%) were women. They did not report any sex difference in tamponade occurrence; however, the overall incidence of tamponade was extremely low (0.3%), and therefore that study was underpowered to answer the question.

Shah et al<sup>1</sup> reported the outcomes of 4156 AF ablations identified from a California state database. They reported a 2.5% incidence of tamponade. Although female sex was associated with increased complication risk, the individual association of female sex and tamponade was not reported. A higher periprocedural complication risk among women was also reported in several other studies<sup>3,4,17</sup> that suggested increased caution and preprocedural discussion of anticipated risk in women.<sup>4</sup> Nevertheless, all the above-referenced studies were



### Number of Tamponades in Females vs. Males



**Meta Analysis**

**Figure 1.** Odds ratio for women compared with men to develop tamponade during atrial fibrillation ablation, among the 19 participating centers, presented as a meta-analysis; combined odds ratio 1.83,  $P < 0.001$ . CI indicates confidence interval.

underpowered to estimate the direct association of sex and tamponade.

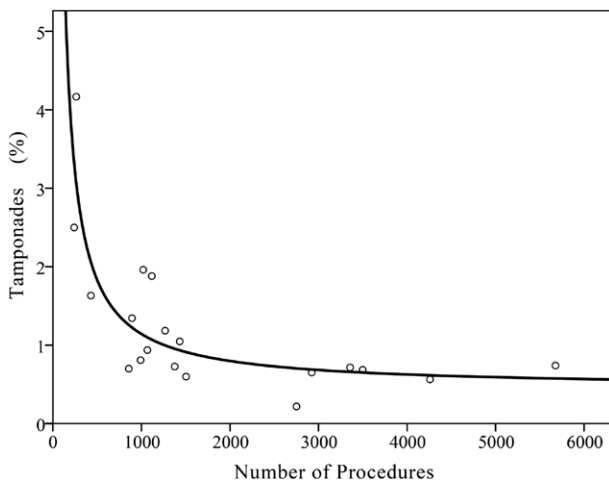
Two large worldwide surveys on AF ablation by Cappato et al<sup>2,6</sup> in 11762 and 20825 ablation procedures found tamponade to be the most common acute complication in 1.2% and 1.3% of patients, respectively. An European survey<sup>7</sup> and a survey among Medicare beneficiaries<sup>18</sup> found tamponade rates of 1.3% and 1.7%, respectively. However, none of these surveys<sup>2,6,7,18</sup> provided data on sex-related complication

differences. In our study, the tamponade rate (0.84%) was lower than that found in worldwide and European surveys. This could be explained by the lower median center volume, at least for the world surveys<sup>2,6</sup> (37 and 275, respectively), as compared with 1267 in our present study.

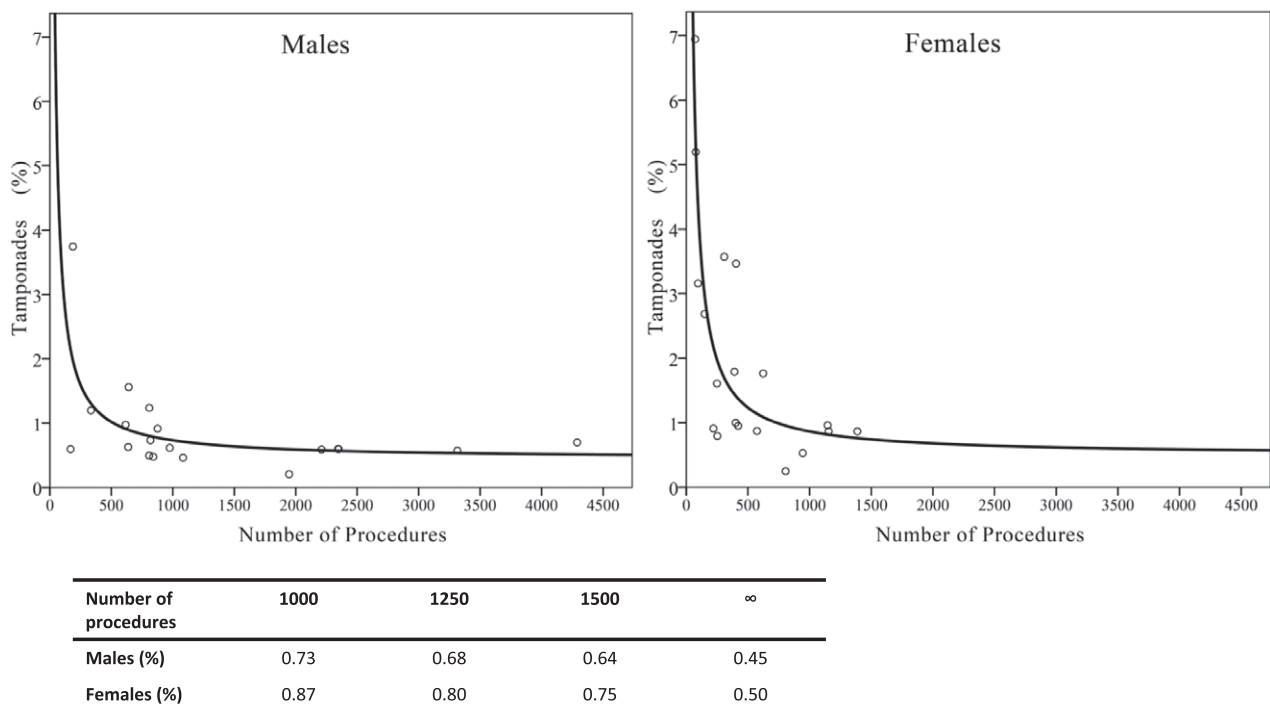
Interestingly, our results demonstrate that the rate of tamponade decreases and is similar after 1000 procedures in men and women (0.87% and 0.73%, respectively). However, because only 25% to 30% of AF ablation procedures (28% in the current study) are performed in women,<sup>12</sup> only centers with total procedural volume of 1390 reach this figure in men compared with centers with procedural volume of 3570 who reach it in women.

**Procedural Characteristics Related to Tamponade**

The lower occurrence of tamponade in high-volume centers is unlikely to be related to different procedural routines among the participating centers. Power settings were overall similar and ICE/transesophageal echocardiography was not used in the majority of centers, including several high-volume centers with low event rates. Of note, few cases of tamponade were preceded by steam pops. Most cases of tamponade (56.2%) were presumably related to catheter manipulation in the left atrium or catheter ablation without sex difference. However, women tended to develop more tamponades during transseptal catheterization. Whether this may be related to a higher incidence of atrial septal aneurysm among women<sup>19</sup> that may render transseptal puncture more difficult and thereby increases the tamponade risk deserves further study. The mechanism of



**Figure 2.** Association between center volume and the risk of tamponade. A reciprocal regression is shown (tamponade rate, 0.45% at  $n = \infty$ ,  $R^2 = 0.713$ ).



**Figure 3.** Upper, Reciprocal regression lines demonstrating the association between center volume and risk of tamponade among men  $R^2=0.355$  and women  $R^2=0.718$ . The lines are shown in a similar scale to simplify comparison. Lower, Estimated tamponade percentage using the fitted curves at  $n=1000$ , 1250, 1500, and  $\infty$  procedures.

higher tamponade risk among women was not explored in the present study. Another possible explanation for increased tamponade risk in women may include thinner left atrial wall and lower atrial volume (which is related to a lower body surface area), especially in patients with AF.<sup>20,21</sup>

### Mode of Management of Tamponade

Our study is the first to report the need for surgery for managing cardiac tamponade in a large-scale multicenter survey, as other reports on the mode of treatment of tamponade originate from smaller single or multicenter series.<sup>5,11,22</sup>

Most cases of tamponade were successfully handled by pericardiocentesis; however, in 16% of cases, surgery was required. In most instances surgery was preceded by pericardiocentesis. In only a minority of cases, surgery was the initial mode of treatment. Again, our results demonstrate that in high-volume centers the percentage of patients requiring surgery was lower. Nevertheless, a curve plot of center volume and the need for surgery demonstrate a non-negligible 10% incidence of patients requiring surgery even in centers performing >4000 ablation procedures. Based on our present results and in agreement with the recent conclusions of the international Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation,<sup>23</sup> we think that centers performing AF ablation should have skill in acute tamponade management including pericardiocentesis and on-site surgical backup. In our study, only 1% of patients died as a consequence of tamponade, and this relatively low incidence rate could be related to the fact that all participating institutions were academic centers with surgical facilities. In contrast, a recent survey of German centers performing AF ablation showed that only 44% of electrophysiological centers performing AF ablation had in-house surgical backup.<sup>24</sup>

### Mortality

In a summarizing analysis of their 2 worldwide surveys, Cappato et al<sup>8</sup> reported an incidence of 0.07% mortality during AF procedures. The most frequent cause of mortality was tamponade (responsible for 25% of deaths) and it occurred in 2% cases of tamponade. In our study, we found a lower incidence of 1% mortality in direct relation with tamponade. As for tamponade, this lower rate of mortality could be related to a larger mean center volume in our study. Also, as stated above, all institutions participating in our survey had surgical facilities. In contrast, the study of Cappato et al<sup>8</sup> did not provide information on the availability of surgical backup for the patients who died because of tamponade, precluding the possibility of further elaborating the role of such backup in a course lethal to their patients.

### Limitations

Participation in our survey was voluntary and the response rate of contributing centers (22%) was relatively low. However, it was similar to that obtained by Cappato et al<sup>2,6</sup> in their surveys (24% and 20%, respectively). If nonresponse bias is large then the reported results need not be significant. Thus, the results while credible require further confirmation. In addition, we cannot assume how many nonrespondent centers were large or small centers.

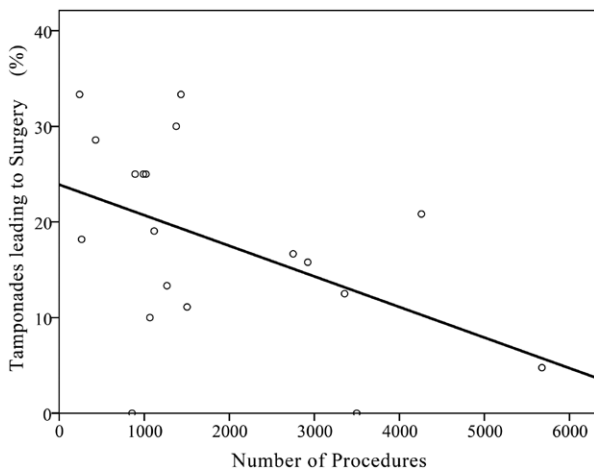
The present study involved many highly skilled academic institutions and therefore the quality of the findings may not be representative of the general population of patients undergoing AF ablation. Moreover, an inherent limitation of surveys is the self-selection involved in response. This may explain the lower rate of tamponade documented in our study as compared with that observed in the Medicare survey<sup>18</sup> and previous reports.<sup>2,6,7</sup>

**Table 2. Cases of Tamponade Managed by Surgery Among the Participating Centers**

Institution	Tamponade	Surgery		Surgery		
		Tamponade n (%)	Men	Men, n (%)	Women, n (%)	
1	6	2 (33)	1	0 (0)	5	2 (40)
2	11	2 (18)	7	2 (29)	4	0 (0)
3	7	2 (28)	4	2 (50)	3	0 (0)
4	6	0 (0)	4	0 (0)	2	0 (0)
5	12	3 (25)	10	2 (20)	2	1 (50)
6	8	2 (25)	4	1 (25)	4	1 (25)
7	20	5 (25)	6	3 (50)	14	2 (14)
8	10	1 (10)	6	0 (0)	4	1 (25)
9	21	4 (19)	10	2 (20)	11	2 (18)
10	15	2 (13)	8	1 (13)	7	1 (14)
11	10	3 (30)	6	2 (33)	4	1 (25)
12	15	5 (33)	4	2 (50)	11	3 (27)
13	9	1 (11)	5	1 (20)	4	0 (0)
14	6	1 (17)	4	1 (25)	2	0 (0)
15	19	3 (16)	14	2 (14)	5	1 (20)
16	24	3 (13)	13	3 (23)	11	0 (0)
17	24	0 (0)	14	0 (0)	10	0 (0)
18	24	5 (21)	19	5 (26)	5	0 (0)
19	42	2 (5)	30	2 (7)	12	0 (0)
Total	289	46 (16)	169	31 (18)	120	15 (13)

Nevertheless, according to our results, we anticipate that the rates of cardiac tamponade and that of tamponade requiring surgery or culminating in death will be even higher in less experienced centers, especially in women.

As this is a large-scale multicenter study we could only gather limited individual patients' characteristics. Therefore, we were unable to evaluate the potential role of individual operator experience and learning curves and distinguish the role of sex from that of associated confounding covariates that



**Figure 4.** Association between the percent of tamponade leading to surgery and center volume. The regression line demonstrates an inverse linear association:  $r=-0.466$ ,  $R^2=0.217$ , and  $P=0.04$ .

may likely be more frequently observed in women (ie, smaller left atrial size, heart size, and body mass index).

Finally, our study focus was on acute cardiac tamponade. It is known that tamponade occurrence and presentation after AF ablation may be delayed  $\leq 45$  days.<sup>25</sup>

**Conclusions**

This large-scale multicenter survey provides evidence for an  $\approx 2$ -fold higher risk of tamponade during AF ablation procedures among women. Yet, the rate of tamponade is low among skilled academic centers. Both sex difference and center experience should be taken in account when obtaining informed patient consent before the procedure. In addition, the availability of immediate surgical backup is advised as a sizable percentage of patients with tamponade may require surgical intervention.

**Disclosures**

None.

**Appendix**

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### CLINICAL PERSPECTIVE

Cardiac tamponade is the most dramatic complication observed during atrial fibrillation (AF) ablation and the leading cause of procedure-related mortality. Whether patient's sex is associated with a different risk for developing this complication is unknown. This large worldwide multicenter study involving 34943 AF ablation procedures was designed to answer this question. The occurrence of tamponade during AF ablation procedures was found to be relatively rare (0.84%); however, women had an 83% higher risk for developing this complication. The risk of developing tamponade was inversely related to center volume with a substantial decrease in women risk in high-volume centers. Surgical management was required in 16% of tamponade cases irrespectively of patient sex, whereas 1% of cases of tamponade resulted in death. To the best of our knowledge this is the largest study evaluating sex difference in the risk of tamponade during AF ablation. Center volume and patient sex should be taken in account when obtaining informed patient consent before the procedure. Also, surgical backup and acute management skills for treating tamponade are important in centers performing AF ablation. Additional research is needed to evaluate the potential role of other different covariates in the risk of tamponade that may likely be more frequently observed in women (ie, smaller left atrial size, heart size, and body mass index).



## SUPPLEMENTAL MATERIAL

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Supplemental Table 1: Presumed mechanism of tamponade in 279 patients from 18 EP centers.

	All patients	Males	Females
Transseptal puncture	30 (10.8%)	11 (6.7%)	19 (16.3%)
Catheter manipulation	64 (22.9%)	35 (21.5%)	29 (25%)
During ablation	93 (33.3%)	59 (36.2%)	34 (29.3%)
Unknown	92 (32.9%)	58 (35.6%)	34 (29.3%)
Total	279	163	116

P=0.046