Impact of body mass index on the outcome of catheter ablation of atrial fibrillation

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ABSTRACT

Objectives The association between obesity and atrial fibrillation (AF) is well-established. We aimed to evaluate the impact of index body mass index (BMI) on AF recurrence at 12 months following catheter ablation using propensity-weighted analysis. In addition, periprocedural complications and fluoroscopy details were examined to assess overall safety in relationship to increasing BMI ranges.

Methods Baseline, periprocedural and follow-up data were collected on consecutive patients scheduled for AF ablation. There were no specific exclusion criteria. Patients were categorised according to baseline BMI in order to assess the outcomes for each category.

Results Among 3333 patients, 728 (21.8%) were classified as normal (BMI <25.0 kg/m2), 1537 (46.1%) as overweight (BMI 25.5–29.0 kg/m2) and 1068 (32.0%) as obese (BMI ≥30.0 kg/m2). Procedural duration and radiation dose were higher for overweight and obese patients compared with those with a normal BMI (p=0.002 and p<0.001, respectively). An index BMI ≥30 kg/m2 led to a 1.2-fold increased likelihood of experiencing recurrent AF at 12-months follow-up as compared with overweight patients (HR 1.223; 95% CI 1.047 to 1.412; p=0.011), while no significant correlation was found between overweight and normal BMI groups (HR 0.954; 95% CI 0.798 to 1.140; p=0.605) and obese versus normal BMI (HR 1.16; 95% CI 0.965 to 1.412; p=0.112).

Conclusions Patients with a baseline BMI ≥30 kg/m2 have a higher recurrence rate of AF following catheter ablation and therefore lifestyle modification to target obesity preprocedure should be considered in these patients.

INTRODUCTION

Catheter ablation of symptomatic atrial fibrillation (AF) is recommended for patients in which medication is either ineffective or not tolerated or in keeping with patient preference for the management of both paroxysmal (Class I, Level of evidence A) and persistent (Class IIa, Level of evidence C) AF.1 Previously, catheter-based intervention has been shown to be more effective than antiarrhythmic drug (AAD) therapy as second-line therapy and compares favourably when used as first-line therapy in paroxysmal AF.2 While it is generally accepted that patients with obesity appear to gain comparable symptomatic improvements following catheter ablation3, some studies have demonstrated an increase in the rate of AF recurrences following catheter ablation4,5 with variable ranges for a body mass index (BMI) over which a reduced efficacy is seen. Other studies have demonstrated that obese patients require more than twice the effective radiation dose as compared with normal-weight patients.6

Additionally, despite the amount of evidence linking obesity and AF, there is a paucity of data to describe the impact of BMI on periprocedural and postprocedural outcomes following catheter ablation. Previous data support a higher periprocedural complication rate for patients with obesity undergoing ablation,7 although these results remain elusive. The Atrial Fibrillation Ablation Registry was conducted by the European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC). Data were collected to assess key features of catheter ablation for AF and the outcomes up to 12 months following the procedure. We therefore sought to determine the impact of obesity on the outcomes for catheter ablation for AF using contemporary large multicentre population data. Our primary objective was to assess the recurrence rate of AF in overweight and obese patients following catheter-based intervention. Our secondary objectives were to determine the impact of BMI at the time of catheter ablation on overall procedural safety and outcomes.

METHODS

Primary objective

To assess the efficacy of catheter ablation, as defined by AF recurrence at 12-months follow-up, in treating obese patients with AF.

Secondary objective

To assess the periprocedural complications, procedure time and radiation dose associated with catheter ablation for overweight and obese patients with AF.

Study design and setting

The AF Ablation Long-Term Registry is a prospective, multicentre, observational registry of...
The 12-month follow-up data of patients enrolled in the in-hospital phase were used for the analyses. Continuous variables were reported as median and IQR. Categorical variables were reported as percentages. Group comparisons were made and a weighted p value <0.05 was considered statistically significant. To reduce the effect of potential confounding bias in an observational study, we also performed rigorous adjustment for differences in patient baseline characteristics using propensity score methods. The underlying propensity model covariates included age (continuous); binary indicators for sex and in-hospital diagnosis of AF; hypertension; diabetes; heart failure; administration of beta-blockers; amiodarone; flecainide; propafenone; dronedarone; quinidine and other antiarrhythmic medication, and CHA2DS2-VASc scores included as continuous variables. Analyses of AF recurrence at 12 months were then performed using Cox proportional hazards models, applying the propensity weights for the adjusted results. Both the unadjusted and the propensity-weighted HR and corresponding 95% CI are presented.

All analyses were performed using SAS statistical software version 9.3 (SAS Institute, Cary, North Carolina, USA). In order to control for potential selection bias, Wald’s confidence limits for an HR were used. The confidence limits for the HR used estimated covariance matrix.

RESULTS

Patient population
Between April 2012 and April 2015, 3630 patients were enrolled in the registry. Participating centres included 64 university hospitals, 23 community/district hospitals and 17 private clinics, with a median number of 585.0 hospital beds (IQR 270.0–978.0). The hospital reference area included a median number of 40,000 inhabitants (IQR 18 544–160 000). The median annual number of AF ablations in the participating centres was 113.0 (IQR 58.0–250.0), with 52 centres performing >100 ablations/year and 17 centres <50 ablations/year.

Baseline clinical characteristics by BMI
Between April 2012 and April 2015, 3333 patients were enrolled into the registry. Baseline characteristics are shown in table 1. Within this cohort, 21.8% study patients had a BMI <25.0 kg/m² (mean BMI 23.1±1.6, 46.1% were overweight (mean BMI 27.3±1.4) and 32.0% of patients were considered obese with a BMI≥30 kg/m² (mean BMI 33.6±3.3). Within the obese category, 8.3% of patients had a BMI>35 kg/m². A significantly higher incidence of diabetes mellitus (p<0.001), hypertension (p<0.001), hypercholesterolaemia (p<0.001) and sleep apnoea (p=0.005) was observed in overweight and obese patients, with the highest proportion of these comorbid conditions observed in those with a BMI>30 kg/m².

Twelve-month follow-up
Complete data for the assessment of 12-month ablation outcomes were available in 2948 patients (87.6%). Twelve-month follow-up evaluations were conducted at a median of 12.4 months (IQR 11.9–13.4) by an in-person clinical visit (52.8%), telephone discussion with the patient (44.2%) or contact with

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Arrhythmias and sudden death
## Table 1 Baseline characteristics of all patients grouped according to BMI: normal BMI, overweight and obese

|                                | All (N=3333) | Normal BMI (BMI<25.0), n=728 | Overweight (BMI 25.0–29.9), n=1537 | P value (overweight versus normal) | Obese (BMI≥30.0), n=1068 | P value (obese versus normal) |
|--------------------------------|--------------|-------------------------------|-----------------------------------|-----------------------------------|--------------------------|-----------------------------|
| Age (years)                    | n            | 3332                          | 728                               | 1537                              | 1067                     | 0.065                       |
|                                | Mean         | 57.9 (10.4)                   | 57.7 (11.9)                       | 58.1 (10.4)                       | 57.6 (9.2)               |                             |
| Females (%)                    | n            | 1065/3333 (32.0)              | 201/728 (36.8)                    | 369/1537 (24.0)                   | 428/1068 (40.1)          | 0.164                       |
| Duration of AF (years)         | n            | 1288                          | 271                               | 620                               | 397                      |                             |
|                                | Median (SD)  | 4.3 (5.2)                     | 4.7 (6.1)                         | 4.5 (5.3)                         | 3.8 (4.1)                |                             |
| CHA2DS2-VASC                   | n            | 3233                          | 692                               | 1499                              | 1042                     | <0.001*                     |
|                                | Median (IQR) | 1.0 (1.0–2.0)                 | 1.0 (0.0–2.0)                     | 1.0 (0.0–2.0)                     | 2.0 (1.0–3.0)            |                             |
| Type of AF (%)                 |              |                               |                                   |                                   |                          |                             |
| Paroxysmal                     | n            | 2239/3333 (67.2)              | 510/728 (70.1)                    | 1061/1537 (69.0)                  | 668/1068 (62.5)          | 0.004*                      |
|                                | Mean (SD)    | 4.3 (5.2)                     | 4.7 (6.1)                         | 4.5 (5.3)                         | 3.8 (4.1)                |                             |
| Persistent                     | n            | 927/3333 (27.8)               | 182/728 (25.0)                    | 409/1537 (26.6)                   | 336/1068 (31.5)          |                             |
| Long-standing persistent       | n            | 167/3333 (5.0)                | 36/728 (4.9)                      | 67/1537 (4.4)                     | 64/1068 (6.0)            |                             |
| Comorbid conditions (%)        |              |                               |                                   |                                   |                          |                             |
| Hypertension                   | n            | 1827/3323 (55.0)              | 275/728 (37.8)                    | 828/1532 (54.0)                   | 724/1064 (68.0)          | <0.001*                     |
|                                | Mean (±SD)   | 59.8 (8.4)                    | 60.3 (8.7)                        | 59.7 (8.7)                        | 59.7 (7.9)               | 0.021                       |
| Diabetes mellitus              | n            | 325/3326 (9.8)                | 31/726 (4.3%)                     | 112/1536 (7.3)                    | 182/1064 (17.1)          | <0.001*                     |
| Hyperlipidaemia                | n            | 1091/3326 (33.4)              | 183/716 (25.6)                    | 502/1510 (33.2)                   | 406/1043 (38.9)          |                             |
| Active smokers                 | n            | 333/3209 (10.4)               | 81/710 (11.4)                     | 156/1479 (10.5)                   | 96/1020 (9.4)            | 0.178                       |
| OSA                            | n            | 113/3070 (3.7)                | 13/689 (1.9)                      | 47/1414 (3.3)                     | 53/967 (5.5)             | <0.001*                     |
| Valvular heart disease         | n            | 372/2263 (16.4)               | 80/399 (20.1%)                    | 183/1029 (17.8%)                  | 109/835 (13.1%)          | 0.001*                      |
| Prior stroke/TIA               | n            | 228/3323 (6.9)                | 48/726 (6.6)                      | 96/1530 (6.3)                     | 84/1067 (7.9)            | 0.316                       |
| Baseline echocardiogram data   |              |                               |                                   |                                   |                          |                             |
| LVEF                           | n            | 2617                          | 551                               | 1200                              | 866                      | 0.021                       |
|                                | Mean (±SD)   | 59.8 (8.4)                    | 60.3 (8.7)                        | 59.7 (8.7)                        | 59.7 (7.9)               |                             |
| LA diameter†                   | n            | 2446                          | 505                               | 1116                              | 825                      |                             |
|                                | Mean (±SD)   | 42.6 (6.6)                    | 40.2 (6.5)                        | 42.2 (6.6)                        | 44.5 (6.2)               | <0.001*                     |
| LVESVi/m²                      | n            | 1499                          | 301                               | 1116                              | 670                      | 0.001*                      |
|                                | Mean (±SD)   | 21.6 (9.9)                    | 21.5 (9.3)                        | 22.1 (10.6)                       | 21.0 (9.1)               |                             |
| LVEDVi/m²                      | n            | 1568                          | 317                               | 698                               | 553                      |                             |
|                                | Mean (±SD)   | 48.8 (17.8)                   | 48.9 (18.1)                       | 49.7 (18.9)                       | 47.6 (16.3)              | <0.001*                     |
| Baseline AAD therapy           |              |                               |                                   |                                   |                          |                             |
| Amiodarone                     | n            | 807/3320 (24.3)               | 142/727 (19.5)                    | 351/1530 (22.9)                   | 314/1063 (29.5)          | <0.001*                     |
| Beta-blockers                  | n            | 11783/3326 (53.6)             | 333/728 (45.7)                    | 823/1532 (53.7)                   | 627/1066 (58.8)          | <0.001*                     |
| Flecainide                     | n            | 548/3328 (16.5)               | 141/728 (19.4)                    | 277/1534 (18.1)                   | 130/1066 (12.2)          | <0.001*                     |
| Propafenone                    | n            | 511/3327 (15.4)               | 104/728 (14.3)                    | 241/1533 (15.7)                   | 166/1066 (15.6)          | 0.454                       |
| Dronedarone                    | n            | 95/3329 (2.9)                 | 24/728 (3.3)                      | 36/1535 (2.3)                     | 35/1066 (3.3)            | 0.988                       |
| Quinidine                      | n            | 5/3328 (0.2)                  | 1/728 (0.1)                       | 3/1534 (0.2)                      | 1/1066 (0.1)             | 1.000                       |
| Disopyramide                   | n            | 8/3328 (0.2)                  | 1/728 (0.1)                       | 5/1534 (0.3)                      | 2/1066 (0.2)             | 1.000                       |
| Other                          | n            | 47/3328 (1.4)                 | 10/728 (1.4)                      | 16/1534 (1.0)                     | 21/1066 (2.0)            | 0.341                       |

*P<0.05.

LA diameter measure in anteroposterior dimensions on TTE.
AAD, antiarrhythmic drug; AF, atrial fibrillation; BMI, body mass index; LA, left atrium; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; OSA, obstructive sleep apnoea; TIA, transient ischaemic attack; TTE, transthoracic echocardiogram.

the patient’s general practitioner (3.0%). Diagnostic methods for the detection of arrhythmia recurrences included periodical clinical visits with ECG (59.7%) and Holter monitoring (64.4%). Transtelephonic monitoring and implanted monitoring systems were only used in 3.5% of cases. A repeat ablation procedure for recurrent AF was undertaken in a total of 636 patients, of which 127 (17.4%), 309 (20.1%) and 200 (18.7%) were classified with normal, overweight and obese BMI indexes, respectively.

**Periprocedural complications**
Procedural details associated with each BMI category are displayed in table 2. The incidence of periprocedural complications was...
similar across all three groups. However, effective radiation dose and overall procedural duration were significantly higher for overweight and obese patients compared with those with a normal BMI (p=0.002 and p<0.001, respectively).

**Ablation strategies and outcome**

The majority of patients underwent a first-time AF ablation procedure (78.3%) with 19.1% requiring a redo procedure for AF and 2.5% for other atrial arrhythmias. There was no significant difference between BMI groups with respect to the proportion of patients undergoing first-time, redo AF or redo atrial tachycardia ablations.

The median procedural duration was significantly higher in overweight (154.0 min, IQR 120.0–200.0) and obese (170.0 min, IQR 120.0–200.2) patients as compared with those with a normal BMI (150.0 min, IQR 115.0–195.0) (p=0.017). Notably, BMI range did not influence the ablation strategies chosen for patients with paroxysmal AF undergoing pulmonary vein isolation (PVI) (table 2). PVI was attempted in 96.3% of all patients, with bidirectional block achieved in 76.5% of patients. For those treated with PVI for paroxysmal AF, linear lesions verification of conduction block was demonstrated in 40.7% of patients who underwent a roof line, 17.3% of patients who underwent a mitral isthmus line, 82.4% of patients who underwent a linear lesion of the posterior wall and 75.0% of patients with any other left atrial linear ablation. There was no significant difference between BMI groups for any of these parameters.

When adverse events of catheter ablation were compared between individuals with a BMI <25 kg m\(^{-2}\) and those with overweight and obese BMI ranges, there was no significant correlation detected between increasing BMI values and the incidence of procedural complications including groin haematoma, pericarditis, cardiac perforation and phrenic nerve palsy.

**BMI as a predictor of AF recurrence**

Before adjustment, obese patients had a 37.7% recurrence of AF at 12-month follow-up compared with 32.3% and 32.4% for normal and overweight patients, respectively. There were 1001 patients (34.1%) with a recurrence of AF, of whom 847 (28.8%) had AF and 162 (5.5%) had atrial flutter.

Following adjustment for selected covariates, the type of AF was independently correlated with AF recurrence, specifically with respect to paroxysmal versus long-standing persistent (HR 0.806; 95% CI 0.696 to 0.934, p=0.004). Additionally, the achievement of entrance and exit block (HR 0.817; 95% CI 0.701 to 0.954, p=0.010) and the postoperative administration of AAD therapy (HR 1.200; 95% CI 1.035 to 1.391, p=0.016)
were significantly correlated with AF recurrence at 12-month follow-up.

**DISCUSSION**

**Main findings**

In the current study, almost half of all patients in this registry were overweight and one-third were classified as obese. Our principle findings are such that a large clinical registry of patients undergoing catheter ablation, obesity was independently associated with AF recurrence at 12 months when compared with being overweight at baseline. In keeping with previous studies, an increase in BMI was associated with increased radiation exposure, though not with an increase in periprocedural complications. There was also a high prevalence of hypertension, diabetes mellitus, structural heart disease and sleep apnoea in patients with an increased BMI at the time of catheter ablation. These conditions are important contributors to AF development and maintenance. Additional factors associated with postprocedural success for patients across all BMI ranges included the presence of paroxysmal rather than persistent AF and a younger age. This is concordant with prior data associating the presence of persistent AF and age as independent factors associated with long-term AF recurrence.13

**AF ablation outcomes and obesity**

Although evidence supports the use of catheter-based ablation for the treatment of patients with arrhythmia, the effect of BMI on AF ablation outcomes remains unclear. To date, studies have demonstrated inconclusive results with respect to procedural outcomes and failure. A meta-analysis involving 5864 individuals demonstrated a 13% greater excess risk of AF recurrence postablation for every 5-unit increase in BMI.14 Other studies have demonstrated an increase in complications among underweight and the morbidly obese, with a paradoxical decrease in complication rates among the moderately obese.14 While numerous reports have also found limited correlation between obesity and ablation complications,15 a recently published study of overweight, obese and morbidly obese patients undergoing catheter ablation revealed a lower success for paroxysmal AF when the BMI was ≥40 kg/m² and for persistent AF when the BMI was ≥35 kg/m².16 In this study, 15.3% of patients had a BMI ≥35 kg/m² compared with only 8.3% in our current study. Although we cannot exclude a selection bias, it is likely that this reflects a European population compared with a North American population where obesity is commonplace.

Likewise, in the largest study of patients undergoing segmental or circumferential PVI, AF was eliminated in 74%, 73% and 69% of lean, overweight and obese patients, respectively. Higher rates of adverse postprocedural events were also observed in higher BMI groups.16 We observed similar associations in our study cohort as AF recurrence rates at follow-up were significantly higher in obese patients when compared with patients with an overweight index BMI. Multivariate weighted analysis validated index BMI as an independent correlate of AF recurrence at 12-month follow-up, with a greater likelihood of recurrence in obese versus overweight patients. This suggests that BMI coupled with other concomitant conditions associated with obesity, such as obstructive sleep apnoea, may be responsible for poorer outcomes following catheter ablation. The fact that there was no significant difference in recurrence rates in obese versus normal BMI suggests that the normal group included those with a low BMI who may have a higher incidence of recurrence and there may be a BMI range closer to what is defined as overweight who have a lower recurrence rate.

Concerning periprocedural complications, no differences in mean fluoroscopy time were observed among BMI groups, whereas radiation exposure was significantly higher in obese and overweight patients as compared with patients with a normal index BMI. This is concordant with previous evidence demonstrating that the amount of radiation exposure for obese patients is more than twice the effective radiation dose than that for patients with a normal BMI.16 Finally, no significant differences in major complications were observed between the various BMI groups undergoing catheter ablation. These results were validated by the large majority of patients achieving freedom from AF without antiarrhythmic agents.
Our results showed that significantly more patients with AF recurrence at 12-month follow-up received AAD therapy following catheter ablation. In a large prospective registry of patients undergoing PVI, the reintroduction of AADs for AF recurrence after ablation resulted in 5-year arrhythmia-free success in up to 70% of 125 patients with multiple failed procedures.17 Identifying certain patient characteristics that predict the maintenance of sinus rhythm following catheter ablation is critical in limiting cardiovascular complications and associated healthcare costs. Since a BMI classification ≥30 kg/m² is correlated with a 1.2-fold increased likelihood of AF recurrence after catheter ablation when compared with overweight patients, the clinical approaches to management of elevated BMI in this population of patients begets further attention.

Obesity is one of the major stimuli for metabolic syndrome and cardiac remodelling, both of which contribute to the propagation and maintenance of AF. In light of suboptimal outcomes, emerging focus has been placed on enhancing the likelihood of success after current surgical treatment or favourably modifying the underlying AF substrate.18 Recent evidence highly suggests that maintained weight loss could be a critical component in reducing AF recurrence rates after index catheter ablation in obese patients.19

Limitations
This registry was based on voluntary participation of all centres. Furthermore, the centres were selected proportionately to the size of the population of the participating countries in order to favour representativeness of the cohort. However, not all contacted centres contributed to the registry in its pilot phase. Conversely, the high rate of response (73%) of contacted centres minimises the risk of an inclusion bias. It should also be highlighted that only medium to high expertise centres were approached and selected. Yet, the participants were followed in national registries with very limited loss to follow-up. The interpretation of 12-month outcomes following catheter ablation is also limited by potential uncontrolled confounders and the lack of homogeneous arrhythmia monitoring. The number of clinical visits and cardiac rhythm monitoring limits the extent of meaningful comparisons between centres.

Missing data did occur in our registry due the fact that it is an observational study and the investigator was not obliged to answer to all questions. Missing data were not included in the analysis of the data.

The ESC-EHRA Long-Term Atrial Fibrillation Ablation Registry still remains the largest international prospective registry evaluating the impact of BMI on arrhythmia recurrences and outcomes following catheter ablation. Therefore, while several noteworthy correlations can be drawn from these results, future studies should focus on ameliorating bias associated with patient selection and extending the clinical follow-up period beyond 12 months.

CONCLUSION
Having an elevated BMI ≥30 kg/m² is independently associated with AF recurrence at 12-month follow-up when compared with having an overweight BMI classification at the time of catheter ablation. Although index BMI is associated with higher effective radiation doses during the procedure, it is not associated with increased rates of procedural complications.

Key messages

What is already known on this subject?
► To date, results have been variable when assessing the potential relationship between an elevated body mass index (BMI) and the outcome from catheter ablation for atrial fibrillation (AF). A recently published single centre retrospective study of overweight, obese and morbidly obese patients undergoing catheter ablation revealed a lower success for paroxysmal AF when the BMI was ≥40 kg/m² and for persistent AF when the BMI was ≥35 kg/m².

What might this study add?
► This is the largest multicentre registry conducted to date examining the association between BMI and the safety and efficacy of radiofrequency catheter ablation for AF. This study shows that obesity increases the recurrence rate of AF following catheter ablation when compared with patients who were overweight. Obesity also increases procedural duration and radiation exposure but not periprocedural complication rates.

How might this impact on clinical practice?
► Catheter ablation should be carefully considered in the treatment of obese patients with AF. Intensive weight loss and lifestyle modification should be recommended to patients in this BMI category prior to performing a catheter ablation.
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