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1 **Comparison of Surgical Ventricular Septal Reduction to Alcohol Septal**
2 **Ablation Therapy in Patients with Hypertrophic Cardiomyopathy**

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Abstract

Ventricular septal myectomy (SM) and alcohol septal ablation (ASA), two septal reduction therapies (SRT), are recommended in symptomatic obstructive hypertrophic cardiomyopathy (HC) despite maximum tolerated medical therapy. Contradictory results between the outcomes of these two types of therapies persist to this day. The objective of this study was to compare in-hospital and mid-term outcomes of SM vs. ASA, at a nationwide level in France. We collected information on patients who underwent SRT for HC using the French nationwide Programme de Médicalisation des Systèmes d'Information (PMSI) database between 2010 and 2019. A total of 1, 574 patients were identified in the database, including 340 patients in the SM arm and 1,234 patients in the ASA arm. No difference during the median follow-up of 1.3 years between the two groups was noted in terms of mortality (adjusted IRR, 0.687 [95% CI, 0.361-1.309]; p = 0.25). However, there was a significantly lower risk of all-cause stroke (adjusted IRR, 0.180 [95% CI, 0.058-0.554]; p = 0.003) in the ASA group. In conclusion, in our “real-life” data from France, mortality after SRT in HC patients was similar after ASA or SM. Moreover, ASA was more widely used than SM despite ESC guidelines recommendations.

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Keywords : Real life; Real world; Hypertrophic cardiomyopathy; Septal reduction therapy

49 **Introduction**

50 Hypertrophic cardiomyopathy (HC) is defined as a hypertrophied myocardium that is not explained by
51 abnormal loading conditions, resulting in ventricular functional and structural impairment with a
52 prevalence of 1 in 500 people in the general population [1,2]. The sarcomeric form is a subtype of HC
53 which can lead to disabling symptoms due to left ventricular outflow tract (LVOT) obstruction. The
54 2014 ESC guidelines are recommending septal reduction therapy (SRT) to improve symptoms in
55 patients with a LVOT gradient of 50 mm Hg in NYHA functional Class III-IV despite maximum tolerated
56 medical therapy. They also recommend as a class I to perform surgical myectomy (SM), rather than
57 alcohol septal ablation (ASA). There is no randomized control trials (RCT) comparing ASA and surgery.
58 However, both interventions seem safe and effective when performed in experienced centres [2-7].
59 Real world trials are using large databases to better analyze the external validity of large RCTs, and are
60 often used to develop new guidelines [8]. There are very few publications of real world data regarding
61 SRT in patients with HC [9,10]. To better describe and compare the safety of the two SRT, we analyzed
62 the events during the follow-up of patients with HC treated with SM or ASA using the French
63 nationwide Programme de Médicalisation des Systèmes d'Information (PMSI) database which
64 provides exhaustive anonymous data for all patients hospitalized in public and private health centres
65 in France.

66

67 **Methods**

68 Our study received the proper ethical oversight. We had an agreement with the CNIL
69 (Commission Nationale de l'Informatique et des Libertés) and the local committee for this type of
70 analysis.

71 The PMSI (Programme de Médicalisation des Systèmes d'Information) is a national database
72 collecting anonymous data of all hospital stays in France, including public and private health centres.
73 This database, established in 2004 and covering the entire French population (67 million inhabitants),

74 offers several interesting data for studying medical practice in real life [8]. It is a nationwide diagnosis-
75 related group based information system in which each hospital stay is coded by the attending physician
76 and includes at least one main diagnosis and the relevant associated diagnoses, procedures, and in-
77 hospital outcome [11]. Primary and secondary diagnoses are coded using the International
78 Classification of Diseases, Tenth Revision (ICD-10), while procedures are coded according to the
79 classification commune des actes médicaux (CCAM) [12]. The PMSI contains the individual anonymized
80 information on each hospitalization that are linked to create a longitudinal record of hospital stays and
81 diagnoses for each patient.

82 The PMSI offers the opportunity to define the current invasive treatment standards and
83 clinical outcomes related to SRT at a nationwide level. Procedures such as SRT in HC by either SM or
84 ASA are documented, as well as the patient comorbidities. The reliability of PMSI data has been
85 evaluated and has also been used in some investigations in the cardiovascular field [13-17].

86 This longitudinal cohort study was derived from the nationwide database using the diagnostic
87 code for HC (I421, I422), either as the main or as an associated diagnosis between 2010 and 2019.
88 243,798 patients were identified by one of these codes in the database. We then identified all the
89 patients in this cohort who underwent either a SM (DAFA006, DAFA007) or an ASA (DDL001). In order
90 to bring out HC related to abnormal loading conditions such as significant aortic stenosis, we excluded
91 all patients that required an intervention on the aortic valve (DBKA 001, DBKA 003, DBKA 006,
92 DBKA 009, DBKA 011, DBMA 001, DBMA 004, DBMA 006, DBMA 009, DBMA 010, DBMA 015). This
93 allowed us to eliminate patients for whom the diagnosis of HC of genetic origin was unlikely, but rather
94 caused by aortic stenosis. Therefore, we believe that the 1574 patients selected represent the
95 population affected by obstructive HC who required SRT in order to improve their symptoms. Baseline
96 characteristics of patients (demographics, comorbidities, medical history, and events during
97 hospitalization or follow-up) with HC treated with SM or ASA seen in French hospitals was identified
98 using data collected in the hospital records. Each variable was identified using ICD-10 codes.

99 SRT can be associated with a number of events. Our primary objective was to compare the
100 incidence of in-hospital mortality after SM or ASA in the last decade. We also aimed to evaluate in-
101 hospital cardiovascular death, all-cause stroke, rehospitalization for heart failure, ventricular
102 tachycardia/ventricular fibrillation/cardiac arrest, atrial fibrillation, major cardiovascular events
103 (cardiovascular death, all-cause stroke or rehospitalization for heart failure) that occurred during the
104 follow-up using the PMSI codes for each patient between January 2010 and December 2019. Pace-
105 maker implantation was also requested. To increase the validation of our analysis, we also assessed
106 the incidence rates of non-cardiovascular deaths and cancer as negative control parameters. The
107 events were identified and collected using their respective ICD-10 codes. Rehospitalization for heart
108 failure was considered when heart failure was recorded as the first diagnosis. The mode of death
109 (cardiovascular or non-cardiovascular) was identified based on the main diagnosis during
110 hospitalization resulting in death based on ICD-10 codes (for cardiovascular death: I00—I99: Diseases
111 of the heart and circulatory system).

112 Qualitative variables are described as frequency, percentages and quantitative variable as
113 median (interquartile). Comparisons were made using chi-square tests for categorical variables and
114 the Mann-Whitney U test for continuous variables. For the analysis, we report incidences for outcomes
115 of interest during the whole follow-up. The number of patients with newly diagnosed outcomes in
116 number per person-time of follow-up in patients treated with SM and in those treated with ASA were
117 compared using Poisson regression to yield an incidence rate ratio (IRR). Multivariable analysis of the
118 primary outcome was also performed using Poisson regression models. We in addition estimated
119 hazard ratios using the model by Fine and Gray for competing risks for all-cause stroke and all-cause
120 death. The adjusted models took into account all the basic variables of **Table 1**. All comparisons with
121 $p < 0.05$ were considered statistically significant. All analyses were performed using Enterprise Guide
122 7.1 (SAS Institute Inc., SAS Campus Drive, Cary, North Carolina) and STATA version 16.0 (Stata Corp,
123 College Station, Texas).

124

125 Results

126 Between 2010 and 2019, 1,574 patients with HC were admitted in public or private hospitals
127 in France and treated with a SRT, including 340 (21.6%) patients treated with SM and 1,234 (78.4%)
128 with ASA. As shown in **Table 1**, patients who underwent ASA were significantly older, less frequently
129 men and had higher rates of previous pacemaker or defibrillator. The SM group shows at baseline more
130 mitral regurgitation, previous endocarditis, previous coronary artery bypass graft and vascular disease.

131 All the events presented were collected in the whole cohort using the respective PMSI coding
132 during the mean follow-up of 2.3 years. All cause of death was recorded in 109 patients with a lower
133 tendency, but not significant, in the first 3 years, in the ASA group with an incidence rate of 2.9%/y
134 versus 3.4%/y in the SM group (adjusted IRR 0.687 [95% CI, 0.361-1.309] $p = 0.25$; **Table 2 and Figure**
135 **1**). The incidence of cardiovascular death also tended to be lower during the first months post
136 procedure in the long run in the ASA group with an incidence rate of 1.2%/y versus 1.9%/y in SM group
137 (adjusted IRR 0.392 [95%CI, 0.156-0.982] $p = 0.05$; **Table 2**). The incidence of non-cardiovascular
138 mortality was similar in the two groups (adjusted IRR 1.033 [95%CI, 0.403-2.646] $p = 0.95$; **Table 2**).
139 The risk of all-cause stroke was significantly lower in the ASA group with an incidence rate of 0.6%/y
140 versus 1.3%/y in the SM group (adjusted IRR 0.180 [95%CI, 0.058-0.554] $p = 0.003$; **Table 2 and**
141 **Figure 2A**), whereas the incidence of new onset of atrial fibrillation, VT/VF/cardiac arrest, major
142 cardiovascular events, and cancer (**Table 2 and Figure 2C**) were not statistically different between the
143 two groups. Interestingly, the risk of rehospitalization for heart failure was not statistically different
144 between the two groups (adjusted IRR 1.228 [95%CI, 0.836-1.806] $p = 0.30$; **Table 2**) but tend to be
145 relatively less frequent with SM after two years of follow-up as shown in **Figure 2B**. We decided to
146 analyze the rate of pacemaker implantation as a secondary endpoint, which showed significantly more
147 pacemaker in the ASA group without too much surprise (adjusted IRR 2.138 [95%CI, 1.600-2.856] $p =$
148 <0.001 ; **Table 2**). All relevant data are within the manuscript. We have performed a propensity match
149 analysis, which showed similar results although having a lower number of patients and statistical
150 power.

151

152 **Discussion**

153 To our knowledge, our study is the largest one comparing mid-term outcomes between SM
154 and ASA in the management of obstructive HC at a French nationwide level based on real life data [3-
155 7,9,10,18]. An adequately powered randomized study powerful enough to address this clinical
156 question would be very difficult, if not impossible. As reported by Olivotto et al., such a study would
157 actually require the initial screening of approximately 35,000 HC patients to recruit over 500 adequate
158 patients for the study in each arm for comparing the outcomes with the two different SRT. This cohort
159 exceeds the total number of patients with HC currently identified in the various global institutions [19].
160 In our longitudinal cohort study, we report mid-term outcomes of all consecutive patients with HC
161 admitted in France between 2010 and 2019 who underwent SRT, either by SM or ASA. Our results
162 showed a significantly higher risk of all-cause stroke and a lower risk tendency of rehospitalization for
163 heart failure in the SM cohort. Moreover, no other significant difference on the incidence of death,
164 cardiovascular death, VT/VF/cardiac arrest, atrial fibrillation or major cardiovascular events were
165 detected between the two groups. An upward trend in the use of ASA compared to SM was identified
166 some years ago despite the guidelines recommendations [1, 10, 20]. Our results show a more frequent
167 use of ASA (n = 1,234) compared to SM (n = 340) to treat that specific population in France. Patients
168 who underwent ASA were older, less frequently men and had higher rates of previous pacemaker or
169 defibrillator. However, they did not demonstrate more comorbidities than patients of the SM group.
170 ASA has practical advantages over SM that could explain more frequent use of the percutaneous
171 approach, such as being relatively less invasive, potentially more widely available, and associated with
172 a short hospital stay [21].

173 Septal myectomy and ASA has demonstrated long-term efficacy and safety in selected high-
174 volume centres with operative mortality rates <1% and procedural mortality of \square 1% respectively [4,
175 18, 22, 23]. When SM is performed outside of experienced centres, the overall mortality can be up to
176 5.2% [10]. Overall long-term survival after SM has been shown to be of 91% at 10 years, and

177 comparable to patients who underwent ASA, as well as to healthy demographic-matched controls [22,
178 23, 24]. All-cause mortality after ASA and SM was comparable and evaluated with an annual risk of
179 mortality around 1.5-2.0% and 1.5% respectively in SRT expertise centres [25, 26]. Our real-life analysis
180 shows an overall comparable mid-term mortality annual incidence rate in both groups. However, we
181 report a slightly higher mortality incidence than those found in high-volume expertise centers. This
182 might be explained by the nationwide analysis of unselected patients unlike a randomized controlled
183 study in more selected patients seen in expert centres. The higher mortality in the surgical group at 6
184 months could also be explained by the inclusion of a lower-volume centres in our analysis.

185 Frequent concerns are raised regarding the creation of a targeted iatrogenic myocardial
186 infarction and its potential for pro-arrhythmia resulting in a negative impact on long-term survival in
187 patients who underwent ASA. In a short series, Folkert and al. observed arrhythmogenic complications
188 in eleven (12%) patients after a mean follow-up of 5 years [27]. This contrasts with our study reporting
189 a low incidence of VT/VF/Cardiac arrest in patients treated with ASA group, which was comparable to
190 that seen in patients treated with SM. The better outcome might be explained by the appropriate
191 selection of the patients undergoing ASA and the development of a better technical performance.

192 More and more data on the periprocedural and long-term outcomes after SRT has recently
193 emerged. All-cause stroke is an outcome frequently studied in the periprocedural stage of SRT by either
194 SM or ASA, but rarely evaluated as a long-term outcome. A 2015 meta-analysis showed similar
195 periprocedural incidence of stroke in both groups at around 1%. A more recent meta-analysis revealed
196 a rate of stroke significantly higher after SM than after ASA (1.5% vs. 0.8%, respectively) [26, 28]. In
197 our study, a significantly higher mid-term incidence of stroke is reported for patients treated with SM.
198 It is interesting to highlight that the incidence of AF was relatively low in the two groups with no
199 significant differences between the two groups, which could suggest that AF may be an unlikely
200 explanation for a higher rate of stroke in one of the two groups. The incidence of AF tended to be
201 higher in the first years after SRT in the SM group. However, it quickly catches up with the ASA group

202 after 2 years of follow-up. This evolution over time could explain that incidence of AF in the first year
203 is more related to postoperative inflammation than an indirect sign of postoperative residual gradient.

204 Although the SM is put forth as the most effective to relieve LVOT obstruction, in recent meta-
205 analysis and in our present cohort study, the occurrence of rehospitalization for heart failure is
206 comparable after SM and ASA [25]. Interestingly, we observed a relatively lower incidence of
207 rehospitalization for heart failure trend in **Figure 2B**, without being significant.

208 Our analysis indicates a low and similar mortality with the two therapies and no other
209 significant differences except for a higher rate of all-cause stroke in the SM cohort and a lower risk
210 tendency of rehospitalization for heart failure with SM. From 2010 through 2019, ASA was more widely
211 used in France than SM despite ESC guidelines recommendations and this increase does not seem to
212 be explained by an aging population with comorbidities. Facing these data, it remains to be asked
213 whether we could consider ASA as a first-line treatment in the idea of a less invasive intervention,
214 potentially more widely available, and associated with a shorter hospital stay.

215 We are aware of the limitations in our study. Real world studies can better analyze the external
216 validity of large RCTs using a large database based on administrative data. The PMSI database contains
217 diagnosis coded using ICD-10 and procedures coded according to the CCAM. An important limitation
218 of our study is related to analysis of large administrative data sets that could be influenced by coding
219 errors. However, the large scale of the database may partly compensate some of these biases. PMSI
220 database collects only in-hospital data and does not offer information regarding patient's medications,
221 echocardiographic variables, and response to therapy. Considering the structure of the database and
222 its analysis, there is no loss to follow up. As a non-randomized, the conclusions for comparisons
223 between SM and ASA should be taken with great caution as we cannot fully exclude the possible
224 confounding variables between the two groups even if a multivariable matching analysis was done.

225 In conclusion, our study is the largest one comparing mid-term outcomes in SM and ASA in HC
226 at a French nationwide level based on real-life data and indicates that the rate of mortality was not

227 different in the two groups. In addition, ASA seems to be more widely used than SM despite ESC
228 guidelines recommendations.

229

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234 **Conflict of interest statement**

235 Conflict of interest: none declared.

- 236 1. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, Hagege AA, Lafont A,
237 Limongelli G, Mahrholdt H, McKenna WJ, Mogensen J, Nihoyannopoulos P, Nistri S, Pieper PG,
238 Pieske B, Rapezzi C, Rutten FH, Tillmanns C, Watkins H. ESC guidelines on diagnosis and
239 management of hypertrophic cardiomyopathy. *Eur Heart J* 2014;35:2733-2779.
- 240 2. Maron B. Clinical course and management of hypertrophic cardiomyopathy. *N Engl J Med*
241 2018;379:655-668.
- 242 3. Nagueh SF, Groves BM, Schwartz L, Smith KM, Wang A, Bach RG, Nielsen C, Leya F, Buegler JM,
243 Rowe SK, Woo A, Maldonado YM, Spencer WH 3rd. Alcohol septal ablation for the treatment of
244 hypertrophic obstructive cardiomyopathy: a multicenter North-American registry. *J Am Coll*
245 *Cardiol* 2011;58:2322-2328.
- 246 4. Veselka J, Lawrenz T, Stellbrink C, Zemanek D, Branny M, Januska J, Groch L, Dimitrow P, Krejci J,
247 Dabrowski M, Mizera S, Kuhn H. Low incidence of procedure-related major adverse cardiac events
248 after alcohol septal ablation for symptomatic hypertrophic obstructive cardiomyopathy. *Can J*
249 *Cardiol* 2013;29:1415-1421.
- 250 5. Sorajja P, Valeti U, Nishimura RA, Ommen SR, Rihal CS, Gersh BJ, Hodge DO, Schaff HV, Holmes DR
251 Jr. Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *Circulation*
252 2008;118:131-139.
- 253 6. Firoozi S, Elliott PM, Sharma S, Murday A, Brecker SJ, Hamid MS, Sachdev B, Thaman R, McKenna
254 WJ. Septal myotomy–myectomy and transcatheter septal alcohol ablation in hypertrophic
255 obstructive cardiomyopathy. A comparison of clinical, haemodynamic and exercise outcomes. *Eur*
256 *Heart J* 2002;23:1617-1624.
- 257 7. Fernandes VL, Nielsen C, Nagueh SF, Herrin AE, Slifka C, Franklin J, Spencer WH 3rd. Follow-up of
258 alcohol septal ablation for symptomatic hypertrophic obstructive cardiomyopathy. The Baylor and
259 Medical University of South Carolina Experience 1996 to 2007. *J Am Coll Cardiol: Cardiovasc Interv*
260 2008;1:561-570.

- 261 8. Moulis G, Lapeyre-Mestre M, Palmaro A, Pugnet G, Montastruc JL, Sailler L. French health
262 insurance databases: What interest for medical research? *Rev Med Interne* 2015;36:411-417.
- 263 9. Panaich SS, Badheka AO, Chothani A, Mehta K, Patel NJ, Deshmukh A, Singh V, Savani GT, Arora S,
264 Patel N, Bhalara V, Grover P, Shah N, Elder M, Mohamad T, Kaki A, Kondur A, Brown M, Grines C,
265 Schreiber T. Results of ventricular septal myectomy and hypertrophic cardiomyopathy (from
266 Nationwide Inpatient Sample [1998–2010]). *Am J Cardiol* 2014;114:1390-1395.
- 267 10. Kim LK, Swaminathan RV, Looser P, Minutello RM, Wong SC, Bergman G, Naidu SS, Gade CL,
268 Charitakis K, Singh HS, Feldman DN. Hospital volume outcomes after septal myectomy and alcohol
269 septal ablation for treatment of obstructive hypertrophic cardiomyopathy: US Nationwide
270 Inpatient Database, 2003–2011. *JAMA Cardiol* 2016;1:324–332.
- 271 11. PMSI. Programme de médicalisation des systèmes d'informations (PMSI).
272 [http://www.drees.sante.gouv.fr/redressements-du-programme-](http://www.drees.sante.gouv.fr/redressements-du-programme-de-medicalisation-des-systemes-d-informations-pmsi)
273 [de-medicalisation-des-](http://www.drees.sante.gouv.fr/redressements-du-programme-de-medicalisation-des-systemes-d-informations-pmsi)
274 [systemes-d-informations-pmsi](http://www.drees.sante.gouv.fr/redressements-du-programme-de-medicalisation-des-systemes-d-informations-pmsi), 2012.
- 275 12. CCAM. Classification commune des actes médicaux (CCAM). [http:// www.ameli.fr/accueil-de-la-](http://www.ameli.fr/accueil-de-la-ccam/trouver-un-acte/index.php)
276 [ccam/trouver-un-acte/index.php](http://www.ameli.fr/accueil-de-la-ccam/trouver-un-acte/index.php). 2012.
- 277 13. Chantry AA, Deneux-Tharoux C, Cans C, Ego A, Quantin C, Bouvier-Colle MH; GRACE study group.
278 Hospital discharge data can be used for monitoring procedures and intensive care related to severe
279 maternal morbidity. *J Clin Epidemiol* 2011;64:1014-1022.
- 280 14. Djennaoui M, Ficheur G, Beuscart R, Chazard E. Improvement of the quality of medical databases:
281 data-mining-based prediction of diagnostic codes from previous patient codes. *Stud Health*
282 *Technol Inform* 2015;210:419-423.
- 283 15. Fauchier L, Clementy N, Pelade C, Collignon C, Nicolle E, Lip GY. Patients with ischemic stroke and
284 incident atrial fibrillation: a nationwide cohort study. *Stroke* 2015;46:2432-2437.
- 285 16. Deharo P, Bisson A, Herbert J, Lacour T, Saint Etienne C, Grammatico-Guillon L, Porto A, Collart F,
286 Bourguignon T, Cuisset T, Fauchier L. Impact of Sapien 3 balloon-expandable versus Evolut R self-

- 286 expandable transcatheter aortic valve implantation in patients with aortic stenosis: data from a
287 nationwide analysis. *Circulation* 2020;141:260-268.
- 288 17. Deharo P, Bisson A, Herbert J, Lacour T, Etienne CS, Porto A, Theron A, Collart F, Bourguignon T,
289 Cuisset T, Fauchier L. Transcatheter Valve-in-Valve Aortic Valve Replacement as an Alternative to
290 Surgical Re-Replacement. *J Am Coll Cardiol* 2020;76:489-499.
- 291 18. Maron BJ, Nishimura RA. Surgical septal myectomy versus alcohol septal ablation. *Circulation*
292 2014;130:1617-1624.
- 293 19. Olivotto I, Ommen SR, Maron MS, Cecchi F, Maron BJ. Surgical myectomy versus alcohol septal
294 ablation for obstructive hypertrophic cardiomyopathy will there ever be a randomized trial? *J Am*
295 *Coll Cardiol* 2007;50:831-834.
- 296 20. Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, Evanovich LL, Hung J, Joglar JA, Kantor
297 P, Kimmelstiel C, Kittleson M, Link MS, Maron MS, Martinez MW, Miyake CY, Schaff HV, Semsarian
298 C, Sorajja P. 2020 AHA/ACC Guideline for the diagnosis and treatment of patients with
299 hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2020;76:e159-e240.
- 300 21. Sorajja P. Alcohol septal ablation for obstructive hypertrophic cardiomyopathy a word of balance.
301 *J Am Coll Cardiol* 2017;70:489-494.
- 302 22. Vanderlaan RD, Woo A, Ralph-Edwards A. Isolated septal myectomy for hypertrophic obstructive
303 cardiomyopathy: an update on the Toronto General Hospital experience. *Ann Cardiothorac Surg*
304 2017;6:364-368.
- 305 23. Rastegar H, Boll G, Rowin EJ, Dolan N, Carroll C, Udelson JE, Wang W, Carpino P, Maron BJ, Maron
306 MS, Chen FY. Results of surgical septal myectomy for obstructive hypertrophic cardiomyopathy:
307 the Tufts experience. *Ann Cardiothorac Surg* 2017;6:353-363.
- 308 24. Sorajja P, Ommen SR, Holmes Jr DR, Dearani JA, Rihal CS, Gersh BJ, Lennon RJ, Nishimura RA.
309 Survival after alcohol septal ablation for obstruc- tive hypertrophic cardiomyopathy. *Circulation*
310 2012;126:2374-2380.

- 311 25. Steggerda RC, Damman K, Balt JC, Liebrechts M, ten Berg JM, van den Berg MP. Periprocedural
312 complications and long-term outcome after alcohol septal ablation versus surgical myectomy in
313 hypertrophic obstructive cardiomyopathy a single-center experience. *J Am Coll Cardiol Cardiovasc*
314 *Interv* 2014;7:1227-1234.
- 315 26. Liebrechts M, Vriesendorp PA, Mahmoodi BK, Schinkel AF, Michels M, ten Berg JM. A systematic
316 review and meta-analysis of long-term outcomes after septal reduction therapy in patients with
317 hypertrophic cardiomyopathy. *J Am Coll Cardiol Heart Fail* 2015;3:896-905.
- 318 27. Ten Cate FJ, Soliman OI, Michels M, Theuns DA, de Jong PL, Geleijnse ML, Serruys PW. Long-term
319 outcome of alcohol septal ablation in patients with obstructive hypertrophic cardiomyopathy.
320 *Circulation Heart Fail* 2010;3:362-369.
- 321 28. Osman M, Kheiri B, Osman K, Barbarawi M, Alhamoud H, Alqahtani F, Alkhouli M. Alcohol septal
322 ablation vs myectomy for symptomatic hypertrophic obstructive cardiomyopathy: Systematic
323 review and meta-analysis. *Clin Cardiol* 2019;42:190-197.
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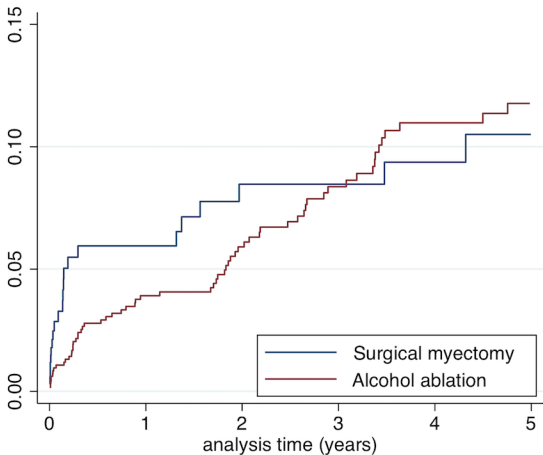
335 **Figure legends**

336 **Figure 1.** Incidences for all-cause death in the patients with HCM treated with surgical myectomy or
337 alcohol septal ablation.

338

339 **Figure 2.** Incidences for all-cause stroke (a), hospitalization for HF (b) and atrial fibrillation (c) in the
340 patients with HCM treated with surgical myectomy or alcohol septal ablation.

341



Number at risk

Surgical myectomy =	338	187	140	122	96	71
Alcohol ablation =	1231	673	508	387	298	225

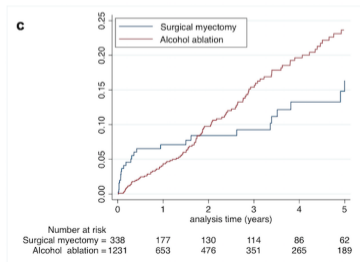
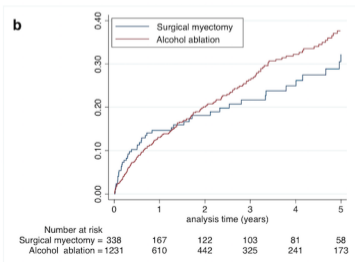
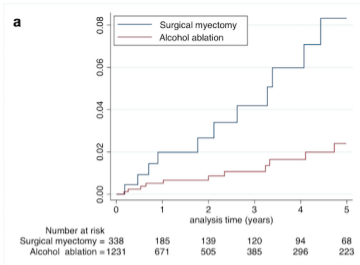


Table 1. Baseline characteristics of patients with hypertrophic cardiomyopathy treated with surgical myectomy or alcohol septal ablation seen in French hospitals (2010-2019)

Variable	Surgical myectomy (n=340)	Alcohol septal ablation (n=1234)	p	Total (n=1574)
Age, years	63 (52-71)	64 (54-73)	0.03	64 (54-72)
Male	195 (57.4%)	597 (48.4%)	0.003	792 (50.4%)
Hypertension	206 (60.6%)	681 (55.2%)	0.08	887 (56.4%)
Diabetes mellitus	53 (15.6%)	147 (11.9%)	0.07	200 (12.7%)
Heart failure	136 (40.0%)	399 (32.3%)	0.01	535 (34.0%)
History of pulmonary edema	39 (11.5%)	36 (2.9%)	<0.0001	75 (4.8%)
Mitral regurgitation	130 (38.2%)	331 (26.8%)	<0.0001	461 (29.3%)
Previous infective endocarditis	10 (2.9%)	6 (0.5%)	0.0001	16 (1.0%)
Coronary artery disease	134 (39.4%)	550 (44.6%)	0.09	684 (43.5%)
Previous myocardial infarction	12 (3.5%)	113 (9.2%)	0.001	125 (8.0%)
Previous percutaneous coronary intervention	26 (7.6%)	181 (14.7%)	0.001	207 (13.2%)
Previous coronary bypass graft	54 (15.9%)	2 (0.2%)	<0.0001	56 (3.6%)
Vascular disease	135 (39.7%)	192 (15.6%)	<0.0001	327 (20.8%)
Left bundle branch block	57 (16.8%)	94 (7.6%)	<0.0001	151 (9.6%)
Right bundle branch block	7 (2.1%)	156 (12.6%)	<0.0001	163 (10.4%)
Atrial fibrillation	153 (45.0%)	276 (22.4%)	<0.0001	429 (27.3%)
Previous VF / sustained VT	26 (7.6%)	113 (9.2%)	0.39	139 (8.8%)
Previous pacemaker or Defibrillator	49 (14.4%)	488 (39.5%)	<0.0001	537 (34.2%)
Implantable Cardiac Defibrillator	7 (2.1%)	49 (4.0%)	0.09	56 (3.6%)
Ischemic stroke	15 (4.4%)	23 (1.9%)	0.01	38 (2.4%)
Smoker	60 (17.6%)	163 (13.2%)	0.04	223 (14.2%)
Dyslipidemia	125 (36.8%)	375 (30.4%)	0.03	500 (31.8%)
Obesity	93 (27.4%)	251 (20.3%)	0.01	344 (21.9%)
Alcohol related diagnoses	14 (4.1%)	41 (3.3%)	0.48	55 (3.5%)
Chronic kidney disease	17 (5.0%)	45 (3.6%)	0.26	62 (3.9%)
Lung disease	61 (17.9%)	153 (12.4%)	0.01	214 (13.6%)
Sleep apnea syndrome	34 (10.0%)	103 (8.3%)	0.34	137 (8.7%)
Chronic obstructive pulmonary disease	29 (8.5%)	85 (6.9%)	0.3	114 (7.3%)
Liver disease	10 (2.9%)	29 (2.4%)	0.54	39 (2.5%)
Gastroesophageal reflux	12 (3.5%)	38 (3.1%)	0.68	50 (3.2%)
Thyroid diseases	29 (8.5%)	105 (8.5%)	0.99	134 (8.5%)
Inflammatory disease	12 (3.5%)	66 (5.3%)	0.17	78 (5.0%)
Anemia	69 (20.3%)	124 (10.0%)	<0.0001	193 (12.3%)
Previous cancer	24 (7.1%)	94 (7.6%)	0.73	118 (7.5%)
Denutrition	13 (3.8%)	54 (4.4%)	0.66	67 (4.3%)
Cognitive impairment	1 (0.3%)	9 (0.7%)	0.37	10 (0.6%)
Illicit drug use	3 (0.9%)	1 (0.1%)	0.01	4 (0.3%)

Values are n (%) or mean±SD. VF = ventricular fibrillation; VT = ventricular tachycardia; SD=standard deviation.

1 **Table 2.** Events during follow-up in patients with hypertrophic cardiomyopathy treated with surgical myectomy or alcohol septal ablation.

Variable	Surgical myectomy (n=340)	Alcohol septal ablation (n=1234)	Hazard ratio for alcohol ablation vs. myectomy (95%CI)	Adjusted hazard ratio for alcohol ablation vs. myectomy (95%CI)	p
Death	28 (3.4%/yr)	81 (2.9%/yr)	0.827 (0.545-1.255)	0.687 (0.361-1.309)	0.25
Cardiovascular death	16 (1.9%/yr)	34 (1.2%/yr)	0.574 (0.325-1.014)	0.392 (0.156-0.982)	0.05
All-cause stroke	11 (1.3%/yr)	17 (0.6%/yr)	0.453 (0.212-0.967)	0.180 (0.058-0.554)	0.003 ‡
Rehospitalization for heart failure	60 (8.4%/yr)	215 (8.9%/yr)	1.061 (0.797-1.412)	1.228 (0.836-1.806)	0.30
VT/VF/Cardiac arrest	11 (1.4%/yr)	35 (1.3%/yr)	0.929 (0.472-1.828)	1.140 (0.436-2.977)	0.79
Atrial fibrillation	29 (3.8%/yr)	135 (5.2%/yr)	1.379 (0.924-2.060)	0.766 (0.433-1.353)	0.36
Major cardiovascular events *	81 (11.5%/yr)	239 (9.9%/yr)	0.844 (0.658-1.084)	0.923 (0.655-1.302)	0.65
Pacemaker implantation	74 (11.0%/yr)	516 (28.5%/yr)	2.408 (1.941-2.989)	2.138 (1.600-2.856)	<0.0001
<i>Negative control analysis</i>					
Non-cardiovascular death	12 (1.4%/yr)	47 (1.7%/yr)	1.206 (0.642-2.268)	1.033 (0.403-2.646)	0.95
Cancer	21 (2.6%/yr)	74 (2.8%/yr)	1.048 (0.646-1.702)	1.534 (0.733-3.209)	0.26

2 Values are n (incidence rate, %/year). CI=confidence interval. * Major cardiovascular events = cardiovascular death, all-cause stroke or
3 rehospitalization for heart failure. ‡ Subhazard ratio = 0.190 (0.061-0.592), p=0.004, by Fine and Gray model for competing risks of stroke and
4 all-cause death. The adjusted model takes into account all the baseline variables of Table 1