Objectives The purpose of this study was to assess the comparative effectiveness and long-term safety of transcatheter versus surgical closure of secundum atrial septal defects (ASD) in adults.

Background Transcatheter ASD closure has largely replaced surgery in most industrialized countries, but long-term data comparing the 2 techniques are limited.

Methods We performed a retrospective population-based cohort study of all patients, ages 18 to 75 years, who had surgical or transcatheter ASD closure in Québec, Canada’s second-largest province, using provincial administrative databases. Primary outcomes were long-term (5-year) reintervention and all-cause mortality. Secondary outcomes were short-term (1-year) onset of congestive heart failure, stroke, or transient ischemic attack, and markers of health service use.

Results Of the 718 ASD closures performed between 1988 and 2005, 383 were surgical and 335 were transcatheter. The long-term reintervention rate was higher in patients with transcatheter ASD closure (7.9% vs. 0.3% at 5 years, p < 0.0038), but the majority of these reinterventions occurred in the first year. Long-term mortality with the transcatheter technique was not inferior to surgical ASD closure (5.3% vs. 6.3% at 5 years, p = 1.00). Secondary outcomes were similar in the 2 groups.

Conclusions Transcatheter ASD closure is associated with a higher long-term reintervention rate and long-term mortality that is not inferior to surgery. Overall, these data support the current practice of using transcatheter ASD closure in the majority of eligible patients and support the decision to intervene on ASD with significant shunts before symptoms become evident. (J Am Coll Cardiol Intv 2013;6:497–503) © 2013 by the American College of Cardiology Foundation.
Long-Term Outcomes After Surgical vs. Transcatheter Closure of ASD in Adults

Kotowycz et al.

**Methods**

**Data sources.** The Québec CHD (Congenital Heart Disease) database is a population-based database of congenital heart disease patients derived from provincial administrative databases that contain comprehensive demographic, diagnostic, and therapeutic records of all patient-linked encounters in Québec, Canada’s second largest province (11). It was created by merging Québec’s physician claims services database (Régie de l’Assurance Maladie du Québec) and the hospital discharge summary database (Med-Écho). By law, attestation of death is sent to the Québec Health Insurance Board, who systematically updates the medical claims database. This makes documentation of death complete in our database, whether it occurred in or out of hospital.

**Study population.** Our study population consisted of all ASD patients between the ages of 18 and 75 years who had surgical or transcatheter ASD closure (Fig. 1). To ensure that we had a population of patients with only secundum ASD, we excluded patients with codes for coexisting congenital anomalies and those who had surgical ASD closure billed in the same day as other cardiac surgeries. We excluded patients with patent foramen ovale (PFO) closure by excluding patients with stroke or transient ischemic attack (TIA) in the year prior to intervention. The Amplatzer septal occluder (AGA Medical, St. Jude Medical, St. Paul, Minnesota) was the only device used for ASD closure during the study period.

**Study design.** This was a retrospective cohort study. Patients having an ASD intervention were followed from the day of intervention until death or end of study on December 31, 2005, whichever occurred first. Our primary outcomes were long-term (5-year) reintervention and all-cause mortality. Our secondary outcomes were short-term (1-year) onset of congestive heart failure (CHF), stroke or TIA, and markers of health service use. For each clinical secondary outcome, we used a subsample of patients who did not have a history of that comorbidity at baseline. The study was approved by our institutional ethics board and the Québec government agency responsible for privacy of access to information.

**Measurements.** Baseline characteristics included age, sex, and the following comorbidities, measured in the 5 years before intervention: coronary artery disease; hypertension; diabetes; CHF; pulmonary hypertension; and atrial fibrillation. Comorbidities were defined using codes from the International Classification of Diseases-Ninth Revision (ICD-9). We also included the Charlson comorbidity index (12), an aggregate measure of patients’ comorbidities that has been used in other epidemiologic studies using administrative data (13,14).

Reintervention was defined as transcatheter ASD closure or surgical ASD closure that occurred during an observation period that started with the day following the index procedure and continued for the duration of follow-up. For...
patients who died during the follow-up period, the date of
death was taken directly from the medical claims database.
The most likely cause of death was determined by reviewing
all patient records in the medical claims and hospital
discharge databases between the day of intervention and the
time of death. The records were independently reviewed by
2 of the authors (M.K. and C.O.) and any disagreements
were resolved by consensus.

Clinical secondary outcomes were defined using ICD-9
diagnostic codes billed in the year following the index
procedure (428.0 to 428.9 for CHF, 430.0 to 435.9 for
stroke/TIA). Markers of health service use (outpatient
physician visits, emergency department visits, days spent in
a critical care unit, and echocardiograms per patient) were
also measured within 1 year of the index procedure, starting
with the first day after discharge from the index hospital-
ization.

Statistical analyses. The primary outcomes of reintervention
and mortality were compared at 30 days, 1 year, and 5 years,
using the chi-square statistic or Fisher exact test. For these
comparisons, we included only the subset of patients who
had at least 30 days, 1 year, or 5 years of follow-up. In
additional analyses for the mortality outcome, we included
all available follow-up for all patients and used Kaplan-
Meier curves and crude and adjusted (for Charlson comor-
bidty index) Cox proportional hazards regression models to
examine time to death. From these analyses, we report
log-rank statistics, hazard ratios (HRs), and 95% confidence
intervals (CIs). Due to the low number of reintervention
outcomes, the estimates from the Cox regression analysis for
reintervention were unstable and are not presented. The
Cox regressions were analyzed as intention-to-treat.

Secondary outcomes at 1-year follow-up were analyzed by
crude and adjusted logistic (clinical outcomes) and Poisson
regression models (health service use outcomes). From the
logistic regression model, we report odds ratios (ORs) and
95% CIs, whereas from the Poisson we report rate ratios
(RRs) and 95% CI. The regression models were adjusted for
the Charlson comorbidity index. All statistical analyses were
carried out using SAS statistical software (version 9.2, SAS

Sensitivity analyses. Given that the rate of our primary
outcomes was low, we were unable to adjust for more than
1 variable at a time. We chose to adjust for the Charlson
index because it provides a composite score of a patient’s
comorbidities. To examine the robustness of our results, we
repeated the primary analysis after adjusting for age and
pulmonary hypertension (which is not captured by the
Charlson index) and after excluding patients who had a
history of pulmonary hypertension. Given the possibility of
a cohort effect, we repeated the analysis by excluding
patients with ASD closure prior to 1998 (the year trans-
catheter closure became available).

Results
Of the 718 patients with ASD closure between 1988 and
2005, 383 were closed surgically and 335 had transcatheter
closure. The number of transcatheter closures grew rapidly
after the technique was introduced, with a corresponding
decrease in the number of surgical closures (Fig. 2). The
baseline characteristics are presented in Table 1. Patients
undergoing transcatheter closure were older and had more
comorbidities. A notable exception was pulmonary hyper-
tension, which was more common in the surgical group.
The median length of follow-up was also longer in the
surgical group (10 years vs. 3 years).

Reintervention rates. There were 2 reinterventions in the
surgical group: the first was a surgical intervention that
occurred on the first post-operative day; and the second was
a transcatheter closure that occurred almost 13 years after
the initial procedure. The reintervention rate in the surgical
group was 1 of 383 (0.3%) after 30 days, and it remained
0.3% after 1 and 5 years of follow-up. The reintervention
rate in the transcatheter group was 6 of 327 (1.8%) after 30
days, 12 of 263 (4.6%) after 1 year, and 3 of 38 (7.9%) after
5 years of follow-up (p = 0.053 for 30 days, p < 0.0001 for
1 year, and p = 0.0038 for 5 years vs. surgical closure). The
majority of reinterventions in the transcatheter group oc-
curred in the first year after closure (Fig. 3). Of the 18
transcatheter patients who required reintervention, 17
(94%) had a surgical reintervention. There were no peripro-
cedural deaths associated with reintervention in these pa-
tients. When we looked at patients who had transcatheter
ASD closure later in the study period (i.e., when operators
had more experience), there was a trend toward a lower
reintervention rate but it was not statistically significant
(data not shown).
Mortality. There were no statistically significant differences in mortality between surgical and transcatheter ASD closure at 30 days (1.0% vs. 0.3%, \( p = 0.38 \)), 1 year (3.2% vs. 0.8%, \( p = 0.053 \)), and 5 years of follow-up (6.3% vs. 5.3%, \( p = 1.00 \)). However, transcatheter ASD closure was associated with lower long-term mortality when evaluated using Kaplan-Meier curves, log-rank statistics, and HR (Fig. 4). The crude mortality rates in the surgical group were 4 of 383 (1.0%) after 30 days, 12 of 380 (3.2%) after 1 year, and 21 of 331 (6.3%) after 5 years of follow-up. The crude mortality rates in the transcatheter group were 1 of 327 (0.3%) after 30 days, 2 of 263 (0.8%) after 1 year, and 2 of 38 (5.3%) after 5 years of follow-up (\( p = 0.38 \) for 30 days, \( p = 0.053 \) for 1 year, and \( p = 1.00 \) for 5 years vs. surgical closure). The unadjusted HR for mortality was 0.278 (95% CI: 0.095 to 0.810) and this persisted after adjusting for the Charlson comorbidity index (HR: 0.161, 95% CI: 0.053 to 0.491). The most likely cause of death for each patient who died within 5 years of ASD closure is presented in Table 2. There appears to be an increase in both procedure-related deaths and long-term deaths in the surgical cohort. The increased number of long-term deaths is likely due to the fact that surgical patients had longer follow-up in the database than transcatheter patients did.

Medical complications and health service use. In the year following ASD closure, there was no difference in the crude rate of new-onset CHF (5.0% vs. 3.0%, \( p = 0.30 \)) or stroke/TIA (1.6% vs. 1.8%, \( p = 0.99 \)) between patients undergoing surgical versus transcatheter ASD closure. The average number of outpatient physician visits per patient (7.5 vs. 6.4, \( p = 0.001 \)) and the average number of critical care days per patient (0.24 vs. 0.14, \( p < 0.001 \)) were higher in the surgical cohort. There was no difference in the average number of emergency department visits between patients in the 2 groups (0.92 vs. 0.98, \( p = 0.61 \)). The number of echocardiograms per patient was higher in the transcatheter group (1.46 vs. 0.63, \( p < 0.001 \)). These data are summarized in Figure 5.

Sensitivity analyses. Mortality findings observed in the Cox analyses (HR: 0.278, 95% CI: 0.095 to 0.810) did not change after adjusting for age (HR: 0.190, 95% CI: 0.065 to 0.558), history of pulmonary hypertension (HR: 0.293, 95% CI: 0.100 to 0.859), or after excluding patients with pulmonary hypertension (HR: 0.234, 95% CI: 0.077 to 0.711). When we excluded patients with ASD closure prior to 1998 (the year transcatheter closure became available), we observed a trend toward reduced mortality in the transcatheter group that was of borderline significance (HR: 0.283, 95% CI: 0.079 to 1.015, \( p = 0.053 \)). There was no difference in the rate of CHF (4.4% vs. 7.4%, \( p = 0.48 \)) or stroke/TIA (2.0% vs. 0%, \( p = 0.58 \)) in patients undergoing surgical closure before versus after 1998.
Discussion

Transcatheter ASD closure has largely replaced surgery in most industrialized countries, despite a paucity of long-term data to support this practice. It is also recommended in patients with significant shunts, even in the absence of symptoms (2). We designed a population-level study to assess the long-term outcomes of transcatheter versus surgical ASD closure. We found that transcatheter closure had a higher reintervention rate than did surgery, and long-term mortality that was at least as good as that of surgery, supporting the current practice of choosing transcatheter closure whenever possible.

Our data show that the proportion of patients undergoing transcatheter ASD closure has grown dramatically since the technique was introduced, suggesting that the threshold for intervention may be lower now that a less-invasive option is available. These findings are in agreement with a U.S. study that showed an increase in the rate of ASD/PFO closures per capita, during the same period (15).

The decision to close an ASD surgically versus using a transcatheter technique is primarily based on technical factors. Transcatheter closure is favored for small ASD with adequate septal rims, whereas surgical closure is preferred when the defect is close to the atrioventricular valves, the coronary sinus, or the venae cavae. Once a decision is made to proceed with transcatheter closure, the technical success rate is reported to be 96% to 98% (5–7). We observed a 30-day reintervention rate of 1.8%, which is in keeping with the literature.

Failure of the transcatheter technique may occur for several reasons. In some cases, there may be a problem with device position or stability, and these patients require

<table>
<thead>
<tr>
<th>Patient Age, yrs</th>
<th>Patient Sex</th>
<th>Time of Death (Days After Closure)</th>
<th>Patients at Risk, n</th>
<th>Cause of Death</th>
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<tr>
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<tr>
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<td>334</td>
<td>Procedural (during index hospitalization)</td>
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<td>61 F</td>
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<td>167</td>
<td>Hypoglycemia</td>
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<td>71 F</td>
<td>906</td>
<td>166</td>
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<td>Surgical closure</td>
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</tr>
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</tr>
<tr>
<td>33 F</td>
<td>3</td>
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</tr>
<tr>
<td>27 F</td>
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<tr>
<td>69 F</td>
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<td>376</td>
<td>Respiratory arrest</td>
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<td>58 F</td>
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<tr>
<td>69 F</td>
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<tr>
<td>62 F</td>
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<td>327</td>
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<td></td>
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<tr>
<td>43 F</td>
<td>1,464</td>
<td>319</td>
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</tbody>
</table>

Most likely causes of death in patients who died within 5 years of ASD closure. 

ASD = atrial septal defect(s).
It remains possible that the differences in long-term mortality appear to be unrelated to the ASD closure itself (Table 2). Although there were more procedure-related deaths in the surgical group, the majority of late deaths in both groups occurred pre-specified time points of 30 days, 1 year, and 5 years. When we excluded patients with ASD closure prior to 1998 (the year transcatheter closure became available), the trend toward reduced mortality persisted but was no longer statistically significant. There was also no significant difference in the rate of these secondary outcomes between the 2 groups.

Study limitations. Our data need to be interpreted in light of the following: This was a retrospective study using administrative databases, where there is potential for misclassification of diagnoses due to coding errors. We addressed this limitation by using very strict exclusion criteria. For example, to exclude patients with coexisting congenital heart disease lesions, we excluded patients with diagnostic codes for those lesions as well as patients who had surgical procedures billed that would imply the existence of those lesions. Furthermore, when the Quebec CHD database was first created, the authors performed manual chart audits to detect and adjust for discrepancies between the data sources (11). Another limitation is that ICD-9 code 745.5 does not differentiate between ASD and PFO. We addressed this limitation by excluding patients who had a stroke or TIA in the year prior to ASD closure because it would be very unusual to close a PFO in Quebec if there was no history of cryptogenic stroke.

This was an observational study, where there is potential for bias due to unmeasured confounding. The decision to close an ASD surgically versus using a transcatheter technique is primarily based on technical factors that cannot be measured with administrative databases. However, it is unlikely that any of these factors are independently associ-
ated with our primary or secondary outcomes, minimizing the potential for bias due to confounding by these factors. There is also a possibility of residual confounding because we were only able to adjust for 1 variable at a time. Thus, it is possible that with higher event rates and longer follow-up, the difference between surgery and intervention would have been less pronounced. Nonetheless, the sensitivity analyses we performed support our main conclusions.

Finally, in all of our analyses, we pooled together subjects who underwent surgery between 1998 and 2005 (when the transcatheter alternative was available) and those who underwent surgery before 1998 in order to increase the sample size and power of our analyses. These 2 groups of patients are different because patients who undergo surgery in the modern era (when there is a transcatheter alternative) tend to have larger ASD or multiple fenestrations and are therefore likely to have larger shunts. However, this decision to pool the groups was taken after preliminary Kaplan-Meier and log-rank analyses showed no difference in re-intervention and mortality between subjects in the surgical cohort who underwent surgery before and after 1998 (data not shown).

Conclusions

We performed a population-level study to assess the outcomes of surgical versus transcatheter ASD closure in a real-world setting. We found that the proportion of patients undergoing transcatheter closure has grown dramatically since the introduction of the technique and it has become the dominant method for closing secundum ASD. Compared with surgical closure, transcatheter ASD closure is associated with a higher reintervention rate in the first year and long-term mortality that is not inferior to surgery. Secondary outcomes were similar between the 2 groups. Overall, our data support the current practice of using transcatheter closure in the majority of eligible patients and support the decision to intervene on ASD with significant shunts before symptoms become evident.

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Key Words: atrial septal defect, cardiac surgery, outcomes, transcatheter.