DEM Journal Club

Article Appraisal

Article: Early or Delayed Cardioversion in Recent-Onset Atrial Fibrillation. NEJM. 2019. 380(16):1499-1508

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Resident Reviewer Name(s) and Residency Affiliation: Dr. Nicholas Monfries (PGY 3 – FRCPC-EM Program)

Faculty Methodology/Bio-statistics Resource Person: Dr. Rob Stenstrom

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Background and Study Objective(s):

Atrial fibrillation is a common condition that is treated in the emergency department. The typical practice in our jurisdiction is to offer a patient who presents to the emergency department with new-onset atrial fibrillation (<48 hours) an electrical or pharmacologic cardioversion. However, there is evidence to suggest that a significant number of patients will spontaneous convert to normal sinus rhythm within the first 24 hours of atrial fibrillation onset, without the need for cardioversion.

The RACE 7 ACWAS trial was a multi-center, non-inferiority trial that investigated whether delayed cardioversion ("wait-and-see" approach) was noninferior to early cardioversion in achieving normal sinus rhythm at a 4-week follow up appointment.

Study Design:

This study was a randomized, non-inferiority trial that took place at 15 emergency departments in the Netherlands (3 academic centers, 8 non-academic teaching hospitals, 4 nonteaching hospitals). Participants were enrolled over a 4-year period (October 2014-September 2018) and included adults (aged 18 years and older) who presented to the ED with hemodynamically stable, symptomatic, and recent onset atrial fibrillation (<36 hours). The participants included patients with first onset or recurrent atrial fibrillation, as well as those without signs of myocardial ischemia. Randomization occurred on a 1:1 ratio between early or delayed cardioversion, using a centralized Web-based system.

The early cardioversion group received pharmacologic cardioversion (preferably with flecainide). Electrical cardioversion was performed on patients who had contraindications to pharmacologic cardioversion, and in those patients who had previous (or current) unsuccessful pharmacologic cardioversion. If a patient was deemed to be high risk for stroke (based on the CHADS-Vasc scale), anticoagulation was started prior to or immediately following cardioversion.

The delayed cardioversion group received rate-control medication (including IV or oral beta-blocking agent, nondihydropyridine calcium-channel blockers, or digoxin). The medication was provided until patients experienced a relief of symptoms and a heart rate of less than 110 bpm. An outpatient clinic appointment was planned for the next day (as close as possible to 48 hours after onset of symptoms). At the clinic appointment, if the patient was still in

atrial fibrillation, they would be referred to the ED for cardioversion.
Regardless of early or delayed cardioversion, all patients received a follow-up appointment at 4 weeks from their initial presentation. At this appointment, an ECG was completed to assess for normal sinus rhythm, as well as a complete medical history was performed. To assess the incidence of recurrences, symptoms, medication use, complications, and repeat hospital visits.

Over the 4-year period, 437 patients were randomized and included in the study protocol. The primary end point was the presence of sinus rhythm at the 4-week trial visit. Secondary end points included recurrent ED visits for atrial fibrillation, duration of the initial ED visit, cardiovascular complications, and time until recurrence of atrial fibrillation.

The authors chose their margin of inferiority as a between-group difference of 10%. It is not clear from the protocol if this number is based on prior studies or author gestalt, but they note that 10% is considered acceptable given the low impact of atrial fibrillation on the patient's prognosis, the availability of good treatment options for atrial fibrillation, and the natural availability in the presence of sinus rhythm.

Results:

The primary analysis was conducted on 427 patients (as 10 patients were lost to follow-up), with 212 patients having undergone delayed cardioversion, and 215 patients having undergone early cardioversion. In addition, telemetric monitoring was completed on aa subgroup of 335 patients to assess time until recurrent atrial fibrillation. With regards to the primary outcome, sinus rhythm was present on ECG at the 4-week visit in 193 patients in the delayed cardioversion group (91%) and 202 patients in the early cardioversion group 94%), equating to a difference of 2.9% (CI:-8.2-2.2 P=0.005). Based on these results, the authors concluded that delayed cardioversion was noninferior to early cardioversion.

With regards to the authors' secondary outcomes, there were not significant differences between the two groups with regards to cardiovascular complications, visits to ED due to atrial fibrillation recurrence, atrial fibrillation recurrence, and quality of life (AFEQT global score).

	Early Cardioversion	Delayed Cardioversion
Visits to ED due to A.Fib Recurrence	14/215 = 7%	14/212 = 7%
Cardiovascular Complications	Transient Ischemic Attack – 1 Acute Coronary Syndrome – 3	Ischemic Stroke – 1 Acute Coronary Syndrome – 3
Mean Duration of Initial ED Visit	158 minutes (Range: 110-228)	120 minutes (Range: 60-253)
Recurrence of A.Fib	50/171 = 29%	49/164 = 30%
Median Time to 1st Recurrence	8 days (Range: 2-18)	12 days (Range: 3-18)

In the delayed cardioversion group, 69% (150/218) of patients spontaneously converted to normal sinus rhythm at the initial clinic visit, without the need for cardioversion. The rate-control agents included beta-blockers (155 patients), calcium-channel blockers (5 patients), digoxin (13 patients), or a combination (1 patient).

Discussion:

This was a multicenter study performed in the Emergency Departments of 15 hospitals in the Netherlands, which are likely similar to our local practice environment. A review of the baseline patient characteristics of the included participants reveals a similar demographic to the atrial fibrillation population we treat in Canada (age 65, predominantly male, with comorbid conditions).

Some key differences between the practice in the study location and our local practice would be with regards to the logistics of cardioversion and the burden of follow-up. In the Netherlands, a cardiologist is required to administer pharmacologic cardioversion agents and an anesthesiologist is required to perform the sedation for an electrical cardioversion. As both of these tasks are with the scope of emergency physicians in Canada, it could be presumed

that cardioversions are less of a time and resource burden in our local practice environment than in the study location. As such, the time and resource benefit of delayed cardioversion stated by the authors is less applicable to our practice.

In addition, access to a follow-up appointment within 48 hours of symptom onset (meaning as little as 12 hours from patient presentation to the ED) could be logistically challenging in our current healthcare system in Canada. In all likelihood, the best place for these patients to follow-up with rapid access to an ECG and expertise with cardioversion (and sedation) would be the emergency department. Therefore, the delayed cardioversion group would likely be contributing to a longer cumulative time spent in the ED, over two visits.

Beyond time and resource benefits, the authors discuss that patients who spontaneously convert to normal sinus rhythm benefit from not having to endure the risks of cardioversion, as well as gain a deeper insight into the management of atrial fibrillation. These posited benefits would likely be similar if this protocol was instituted in our practice environment, though it would have been interesting to have seen the data on the rate of cardioversion complications.

A final note should be made regarding stroke risk. While the study population did not experience a difference in the occurrence of cerebral vascular disease between early and delayed cardioversion, the study is not powered to make a conclusion about this difference. It would be insightful to have a study that compares the risk of a cerebral vascular event in delayed vs. early cardioversion.

The Bottom Line:

This was a well-designed and executed study that concluded that delayed cardioversion is non-inferior to early cardioversion. However, the benefits of delayed cardioversion are less applicable to our practice environment, as cardioversions are less of a burden on time and resources due to the wider scope of practice of emergency medicine. In addition, further research is needed to better understand the risks of CVA in delaying cardioversion. Based on the discussion with the attending emergency physicians and residents at our local journal club, this article is unlikely to change practice at this point in time.