Critical Review Form
Therapy

Ortiz M, Martín A, Arribas F, Coll-Vinent B, Del Arco C, Peinado R, Almendral J; PROCAMIO Study Investigators. Randomized comparison of intravenous procainamide vs. intravenous amiodarone for the acute treatment of tolerated wide QRS tachycardia: the PROCAMIO study. Eur Heart J. 2017 May 1;38(17):1329-1335.

Objectives: **To compare "the safety and efficacy of intravenous procainamide and amiodarone in the acute treatment of wide QRS complex monomorphic tachycardias (presumably VT) which are haemodynamically well tolerated." (p. 1330)**

Methods: **This prospective, multicenter, randomized, open-label trial was conducted at 29 hospitals in Spain over a six-year period. Hemodynamically stable patients with tachycardia with a wide QRS complex who required medical attention were randomized to receive either IV procainamide (10 mg/kg over 20 minutes) or IV amiodarone (5 mg/kg over 20 minutes). Inclusion criteria were:**

1. **Regular heart rhythm with a rate ≥ 120 bpm**
2. **QRS ≥ 120**
3. **Systolic blood pressure ≥ 90 mmHg**
4. **Absence of dyspnea at rest**
5. **Absence of signs of peripheral hypoperfusion**
6. **Absence of severe anginal symptoms**
7. **Age > 18.**

Patients felt to have supraventricular tachycardia by physician criteria, those receiving IV amiodarone or procainamide in the prior 24 hours, and those with contraindications to the study drugs were excluded.

The 40-minute "study period" was defined as the 20 minutes during which the drug was administered and 20 minutes following completion of administration. All patients were observed for 24 hours following study drug administration. The primary outcome was major cardiac adverse events, defined as any of the following

1) **Clinical signs of peripheral hypoperfusion**
2) **Dyspnea at rest or orthopnea with signs of pulmonary congestion**
3) **Severe hypotension (SBP ≤ 70 if the pretreatment SBP was ≤ 100 or SBP ≤ 80 if the pretreatment SBP was > 100)**
4) **Acceleration of HR > 20 bpm of its mean value; or 5) development of polymorphic ventricular tachycardia.**

Secondary outcomes included acute termination of the tachycardia episode during the "study period" and total adverse events.

There were 74 patients recruited at 16 of the 29 participating hospitals, of whom 12 were excluded, leaving 62 patients in the final analysis. Thirty-three patients were randomized to receive procainamide and 29 were randomized to receive amiodarone.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes: "groups of 10 numbered and closed envelopes were deposited at each Centre (and were replaced as necessary) so, whenever a candidate appeared, the investigator could open the next envelope containing the assigned therapy." (p. 1330)
2.	Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Likely yes. The authors do not specifically mention that the envelopes were opaque, suggesting the possibility that randomization would be subverted. In addition, it is not clear who prepared and delivered the envelopes to the study sites.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. Only patient (in the amiodarone group) did not receive the assigned intervention. This was, therefore, an intention to treat analysis.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, history of cardiac disease, baseline vital signs, and baseline labs. Patients in the procainamide group were more like to receive adenosine in the ED (12% vs. 0%), and patients in the amiodarone group were more likely to have received previous treatment with oral amiodarone (17% vs. 0%).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Yes. This study was not blinded, though it seems unlikely that performance bias on the part of the patients would have had much effect on the outcomes.
2.	Were clinicians aware of group allocation?	Yes. Given the possibility of additional interventions ordered by the treating clinicians (e.g. IV fluids, electrolyte repletion), it is quite possible that some degree of performance bias on

		the part of the clinicians could have affected the outcomes.
3.	Were outcome assessors aware of group allocation?	No. "Adverse events were analysed and classified blinded to the patient study group." (p. 1330). In addition, the outcomes were precisely defined and hence fairly objective.
4.	Was follow-up complete?	Yes. The outcomes in the study were measured during a fairly brief "study period" of 40 minutes, and outcomes were available for all patients analyzed.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• Major cardiac events were less common among patients treated with procainamide compared to those treated with amiodarone: 9% vs. 41%, OR 0.1 (95% CI 0.03 to 0.6). The most common adverse event was hypotension requiring immediate electrical cardioversion. There were no deaths in either group. • Termination of ventricular tachycardia occurred more often in patients receiving procainamide: 67% vs 38%, OR 3.3 (95% CI 1.2 to 9.3). • Total adverse events during the "study period" were less common in the procainamide group compared to the amiodarone group: 24% vs. 48%, OR 0.34 (95% CI 0.12 to 1.00). • Adverse events during the observation period were slightly less common in the procainamide group versus the amiodarone group, though this did not achieve statistical significance: 18% vs. 31%, OR 0.49 (95% CI 0.15 to 1.61).
2.	How precise was the estimate of the treatment effect?	See above. Despite the small sample size, the confidence intervals were fairly narrow due to the high incidence of the outcomes.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Likely yes. While this study was conducted in Spain, and while it is possible that a different racial makeup of patients was enrolled, these were still patients with hemodynamically stable ventricular tachycardia, and would likely respond

		to the study medications in a similar fashion to patients treated in our institution (external validity).
2.	Were all clinically important outcomes considered?	No. While the primary outcome (major cardiac adverse events) is quite important to understanding the safety of these medications, the assessment of efficacy was done over a very short timeframe (20 minutes following completion of drug administration). While there is no consensus on how long to wait for chemical cardioversion to occur, twenty minutes does not seem like an adequate duration of observation.
3.	Are the likely treatment benefits worth the potential harm and costs?	No. It would seem that procainamide is a much safer medication when administered for hemodynamically stable ventricular tachycardia, with a much higher incidence of significant hypotension observed among those patients receiving amiodarone. In addition, while not the primary outcome being studied, procainamide also resulted in successful cardioversion nearly twice as often as amiodarone.

Limitations:

1. **The authors did not report the dates of study.**

2. **Only about a fifth of the number of planned patients were actually enrolled. The study was stopped early due to low and declining enrollment. In addition, patients were only enrolled from 16 of the 29 participating centers. These findings suggest there may have been some degree of selection bias with regards to enrollment.**

3. **The authors did not specify if opaque envelopes were used for randomization, and provide no information regarding who prepared the envelopes and how they were delivered to the study sites. Without knowing these things, it is difficult to assess the quality of allocation concealment.**

4. **This was an open-label study, and while it is doubtful that any degree of performance bias on the part of the patients would have affected the outcomes, clinicians may well have treated patients differently based on the medication being administered.**

Bottom Line:

This small, open-label, randomized study demonstrated significantly fewer major cardiac adverse events with the administration of IV procainamide for hemodynamically stable ventricular tachycardia compared to administration of IV amiodarone (OR 0.1; 95% CI 0.03 to 0.6). In addition, a much higher rate of

chemical cardioversion was achieved with procainamide compared to amiodarone (OR 3.3; 95% CI 1.2 to 9.3). Despite some limitations, including low enrollment and the possibility of performance bias, procainamide does appear to be superior to amiodarone in the management of stable ventricular tachycardia.