

Patent Foramen Ovale: Stroke and Migraine Headache Associations

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Introduction

- ✓ Patent Foramen Ovale (PFO) is associated with a number of clinical syndromes
 - ✓ Thromboembolic Stroke / TIA
 - ✓ Migraine Headache
 - ✓ Decompression Illness in Divers
 - ✓ Cyanosis
 - ✓ Systemic (non-cerebral) infarct
 - ✓ Obstructive Sleep Apnea



PFO / Stroke - Migraine

- ✓ There is no prospective randomized data to prove that closure of a PFO is beneficial in preventing either stroke or migraine headache.
- ✓ Clinical trials are in progress to try to prove the value of such therapy
- ✓ Need to examine existing literature

Patent Foramen Ovale

✓ **Thromboembolic Stroke**



PFO / Stroke - TIA

✓ Not in dispute:

- In stroke pts < 55 yrs old, no other source, prevalence of PFO is 41-60% compared with 20 – 25% in the general population
- PFO is a strong risk factor for recurrent stroke (3 – 15% annual risk)



PFO: Stroke - TIA

✓ Not in dispute:

- In pts with recurrent stroke despite anticoagulation, PFO closure is appropriate
- Until evidence proves otherwise, in pts with incidental finding of PFO, closure is INAPPROPRIATE



PFO: Stroke - TIA

✓ “To close or not to close?”



PFO / Stroke

✓ PFO not a risk:

Effect of Medical Treatment in Stroke Patients With Patent Foramen Ovale

Patent Foramen Ovale in Cryptogenic Stroke Study

Shunichi Homma, MD; Ralph L. Sacco, MD, MS; Marco R. Di Tullio, MD; Robert R. Sciacca, EngScD; J.P. Mohr, MD; for the PFO in Cryptogenic Stroke Study (PICSS) Investigators*

Circulation 2002;105:2625-2631



PFO / Stroke

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- ✓ “On medical therapy, the presence of PFO did not increase the chance of adverse events...”



PFO / Stroke

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✓ Strengths:

- Prospective data collection, close follow-up



PFO / Stroke

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✓ Weaknesses

- Non-comparison with closure
- Only 98 PFO/cryptogenic stroke patients
- Based on 14 events



PFO / Stroke

✓ Don't close it:

AHA/ASA Guideline

Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Council on Stroke

Co-Sponsored by the Council on Cardiovascular Radiology and Intervention

The American Academy of Neurology affirms the value of this guideline.

Ralph L. Sacco, MD, MS, FAHA, FAAN, Chair; Robert Adams, MD, FAHA, Vice Chair, Greg Albers, MD; Mark J. Alberts, MD, FAHA; Oscar Benavente, MD; Karen Furie, MD, MPH, FAHA; Larry B. Goldstein, MD, FAHA, FAAN; Philip Gorelick, MD, MPH, FAHA, FAAN; Jonathan Halperin, MD, FAHA; Robert Harbaugh, MD, FACS, FAHA; S. Claiborne Johnston, MD, PhD; Irene Katzan, MD, FAHA; Margaret Kelly-Hayes, RN, EdD, FAHA; Edgar J. Kenton, MD, FAHA, FAAN; Michael Marks, MD; Lee H. Schwamm, MD, FAHA; Thomas Tomsick, MD, FAHA

Circulation 2006;113:e409 – e449.



PFO / Stroke

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✓ “Insufficient data exist to make a recommendation about PFO closure in patients with a first stroke”



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✓ “PFO closure may be considered for patients with recurrent cryptogenic stroke despite optimal medical therapy.”



PFO / Stroke

✓ Definitely close it:

Secondary prevention after cryptogenic cerebrovascular events
in patients with patent foramen ovale[☆]

Herwig Walter Schuchlenz^{a,*}, Wolfgang Weihs^a, Andrea Berghold^b,
Anita Lechner^c, Reinhold Schmidt^c

^a*Medical Department II, LKH Graz-West, Graz, Austria*

^b*Institute for Medical Informatics, Statistics and Documentation, Karl Franzens University, Graz, Austria*

^c*Department of Neurology, Karl-Franzens University, Graz, Austria*

Int J Cardiol 2005;101:77 - 82.

PFO / Stroke

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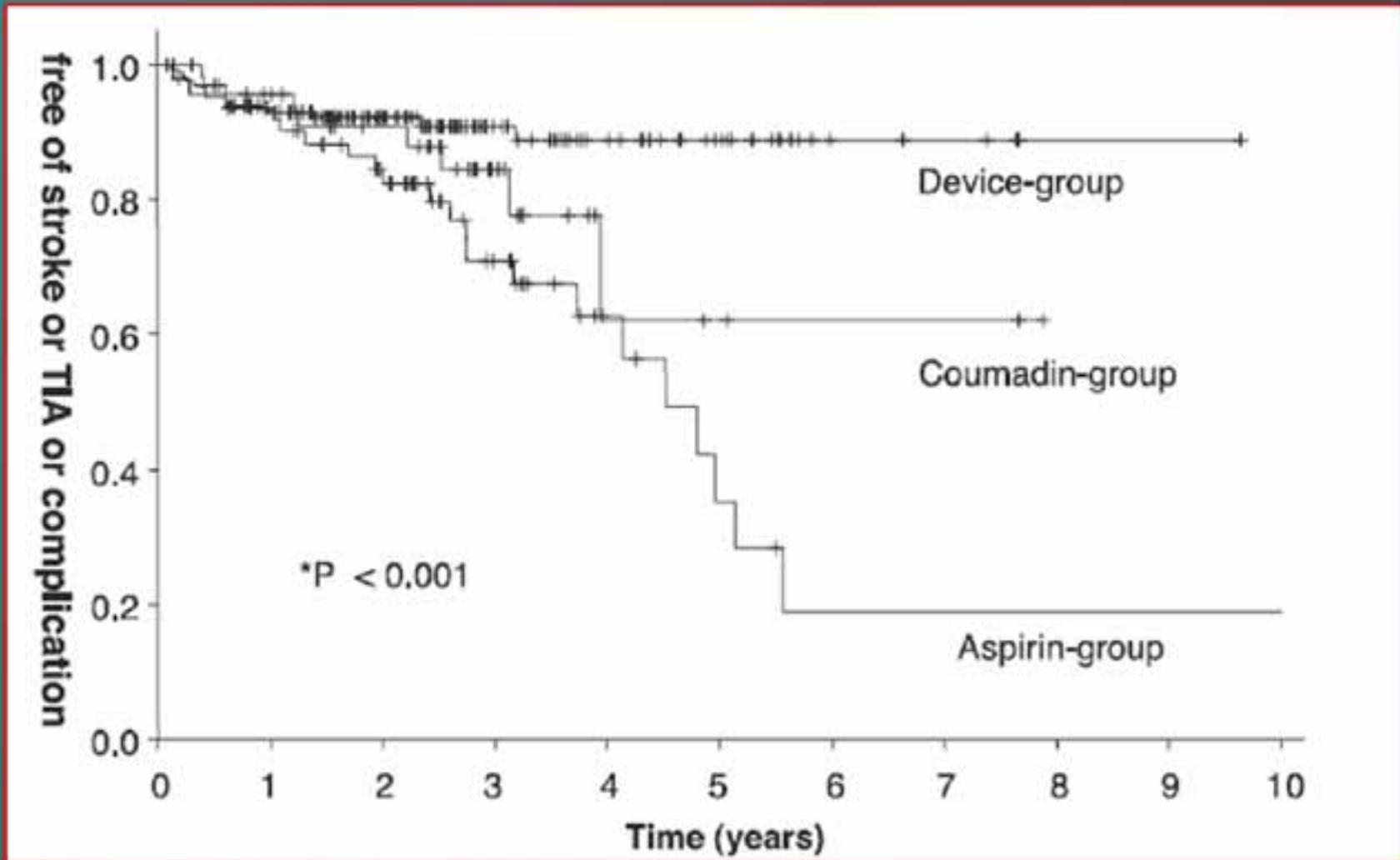
^bInstitute for Medical Informatics, Statistics and Documentation, Karl-Franzens University, Graz, Austria

^cDepartment of Neurology, Karl-Franzens University, Graz, Austria

- ✓ “Risk of [stroke] recurrence was lower after device closure of the patent foramen ovale.”

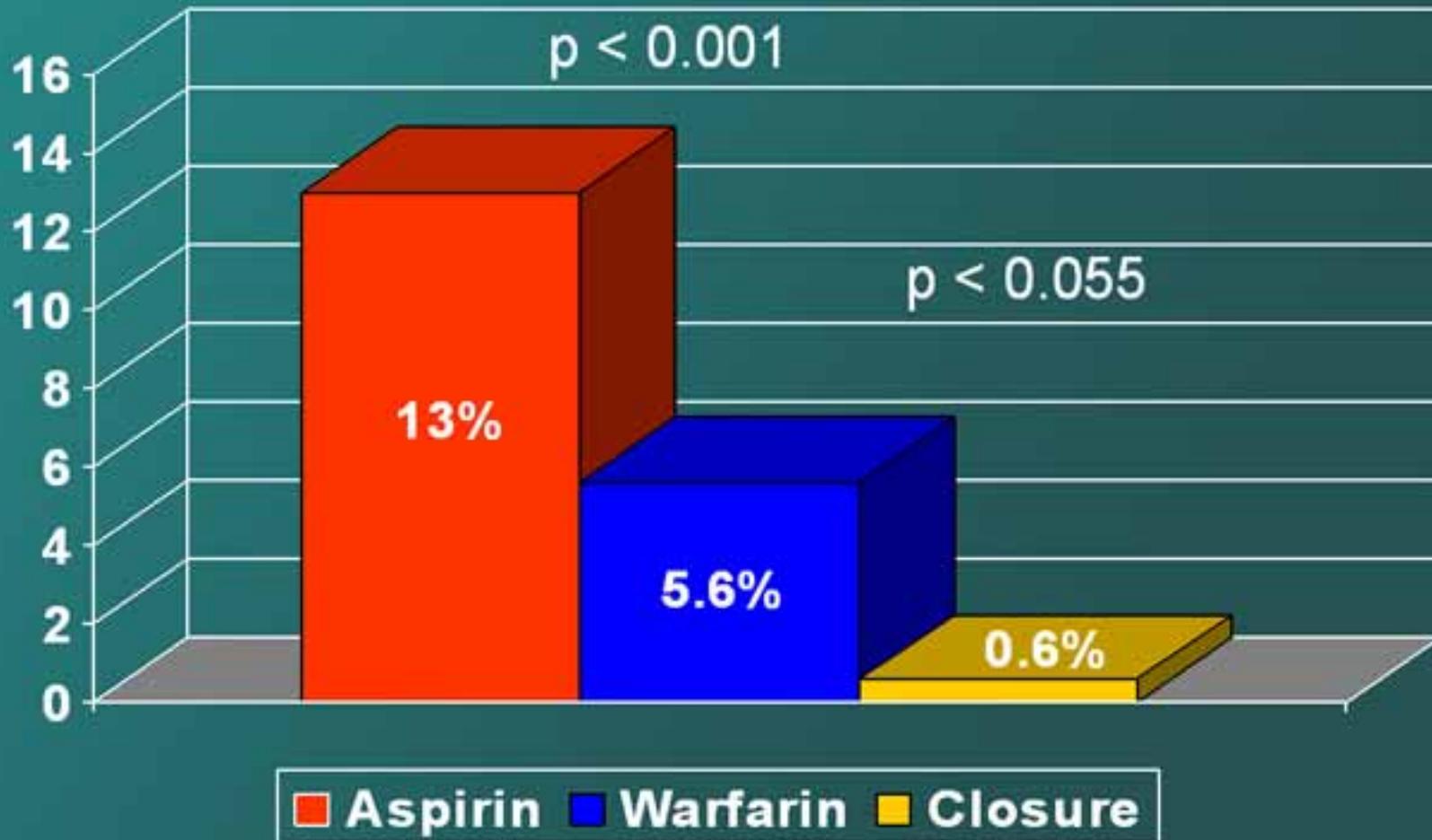


Schuchlenz et al (2005)



Schuchlenz et al (2005)

Annual Recurrence Rate



PFO / Stroke

Secondary prevention after cryptogenic cerebrovascular events
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✓ Strengths

- Prospective data collection
- Direct comparison of three therapies: 167 closure, 66 ASA, 47 warfarin
- Up to 8 year follow-up

PFO / Stroke

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- ✓ Weaknesses
 - Non-randomized therapy
 - Multiple devices used in closure arm

PFO / Stroke

✓ Prospective, Randomized Studies

- CLOSURE I: NMT Medical
- RESPECT: AGA Medical



Patent Foramen Ovale

✓ **Migraine Headache**

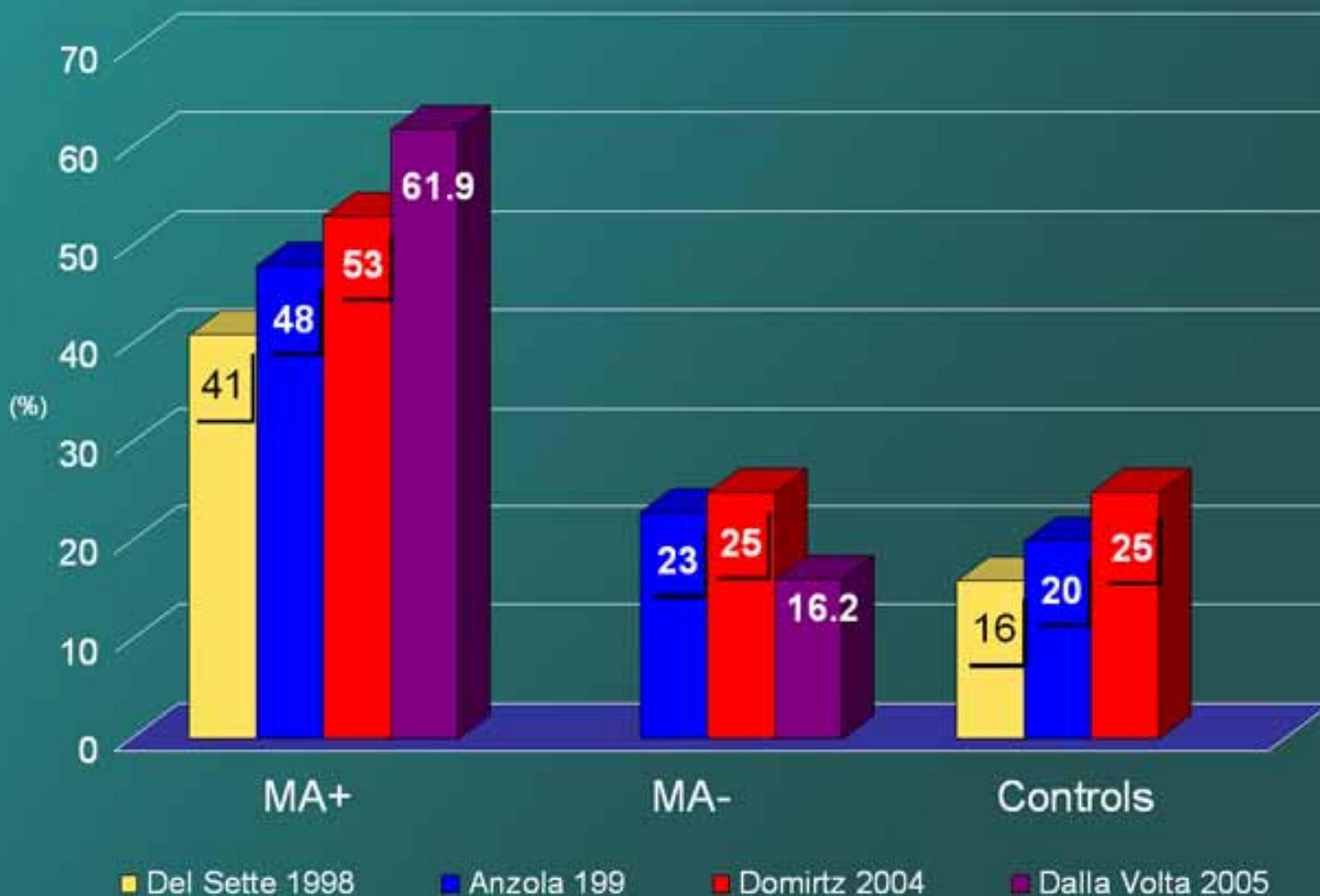
PFO / Migraine Headache

✓ Not in dispute:

- A history of migraine headache is strongly associated with the presence of patent foramen ovale and right to left shunt
- There is no known mechanism relating PFO and migraines
- Reduction in migraines observed after PFO closure in stroke pts

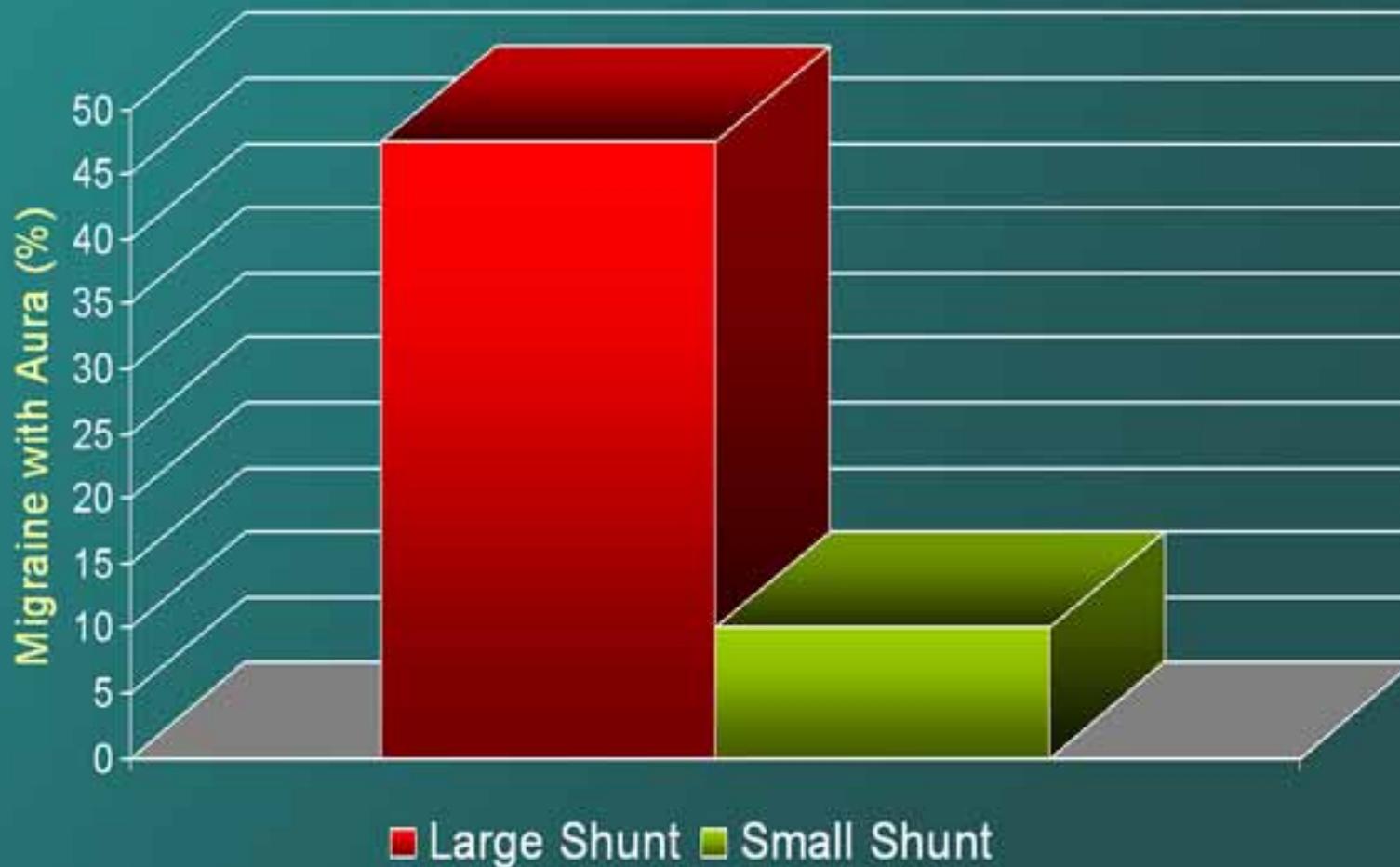


PFO: Prevalence in Migraineurs



PFO / Migraine: Shunt size

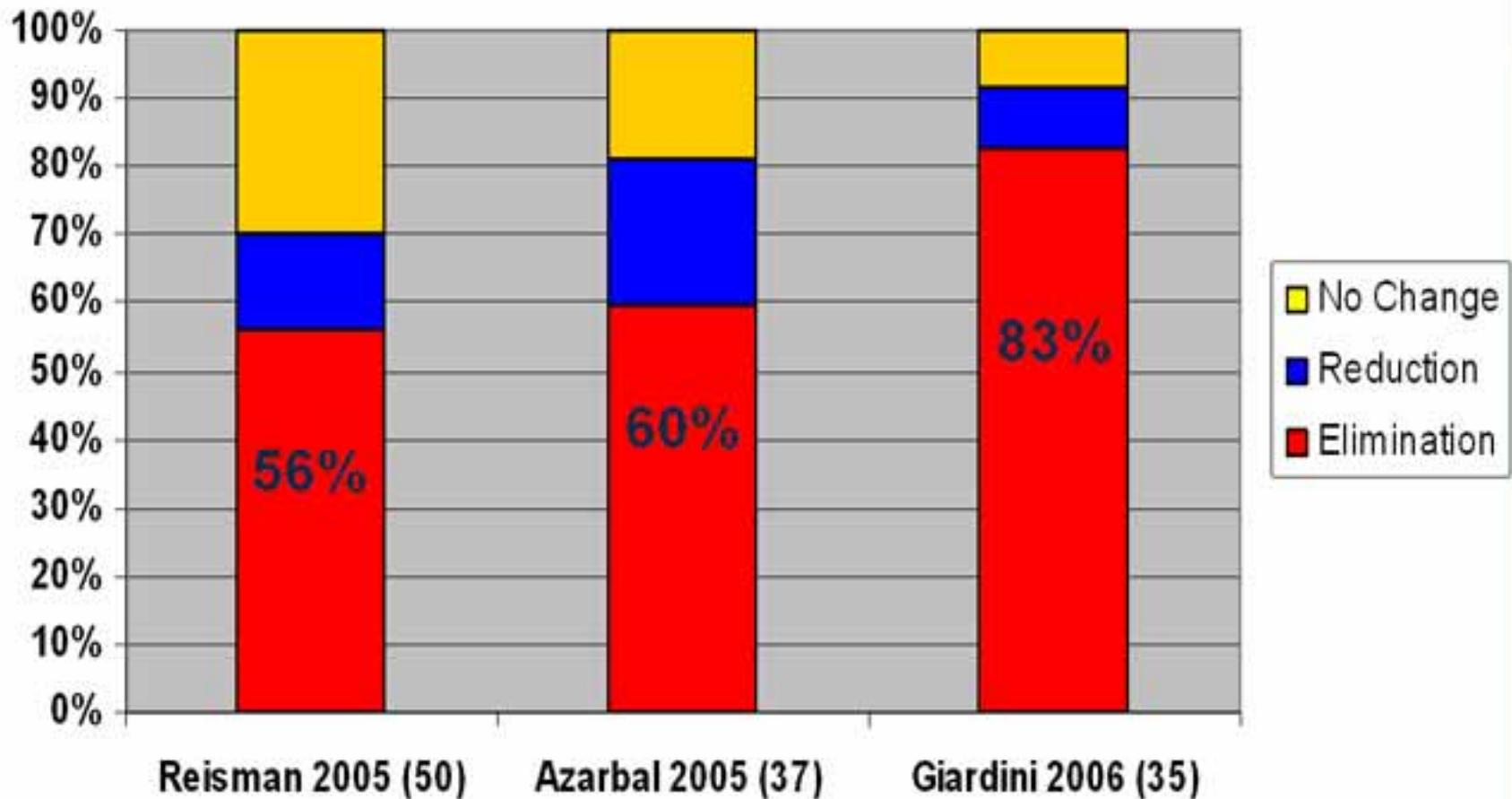
120 divers with PFO / Migraine with aura



Wilmshurst P et al. Clin Sci 2001;100:215-20



Migraine Relief after PFO Closure



Migraine Headache

✓ Prospective Clinical Trial:

- **MIST I:**
 - 147 Migraine with Aura pts, randomized 1:1 for closure (STARFlex) and for sham catheterization
 - All pts had failed medical treatment
 - No elimination of headaches
 - 42% pts had >50% reduction in headache compared with 23% of controls ($p < 0.05$)



Migraine Headache

- ✓ **Enrolling Clinical Trials: US 2006**
 - St. Jude's Trial (ESCAPE)
 - NMT Trial (MIST II)
 - AGA Trial (PREMIUM)
 - Cierra Trial (PARADIGM)



Conclusions

- ✓ **Non-randomized data exists to support closure of PFO**
- ✓ **Need to complete definitive studies to have any hope of consensus on these complex issues**

