WHY RCTs & GUIDELINES ARE OFTEN MISLEADING: HOW TO MAKE A PROPER DECISION

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CACVS 2017

PARIS – JANUARY 20, 2017

I HAVE NO
FINANCIAL CONFLICTS
BUT LOTS OF BIASES

2 PILLARS OF MEDICINE THAT INFLUENCE PRACTICE

1. RCTs
2. GUIDELINES

MY GOAL TODAY

SHOW YOU THAT BOTH THESE PILLARS ARE FLAWED & WHY

RCTs

PEER REVIEWED ARTICLES IN LEADING JOURNALS INFLUENCE MEDICAL PRACTICE

THESE JOURNALS – LIKE NEJM, LANCET JAMA, CIRCULATION, JVS, BMJ, ETC ARE BASIS OF OUR WORK – BIBLE OF VS

ASSUMED THAT THEY ARE PEER REVIEWED & EDITED WITH OBJECTIVITY & THAT THEIR CONTENT IS UNBIASED & REFLECTS TRUTH

IN THESE JOURNALS RC TRIALS = LEVEL I EVIDENCE - IS THE "HOLY GRAIL" – OR AS CLOSE TO THE TRUTH AS IT GETS

DEEMED BEST POSSIBLE BASIS FOR MEDICAL PRACTICE

SHOW WHY THIS IS NOT SO !

RCTs – EVEN IN LEADING JOURNALS CAN BE MISLEADING & WRONG BECAUSE OF:

i FLAWS IN RCTs

ii EVEN GOOD RCTs CAN BE MISINTERPRETED & THUS RENDERED MISLEADING

EXAMPLES: CREST, IMPROVE

Veith: How can good RCTs in leading journals be so misinterpreted. J Vasc Surg 2013;57S:3s-7s

Veith, Rockman: Recent EVAR vs OR RCTs for RAAAs are misleading. VASCULAR 2015; 23:217–219

IMPROVE TRIAL

CAREFULLY DONE

LARGE MULTICENTER RCT -
30-DAY & 1-YEAR RESULTS PUBLISHED

Its main conclusion was that:

"A strategy of endovascular repair was not associated with significant reduction in 30 day or 1 year mortality"

THIS CONCLUSION WAS…

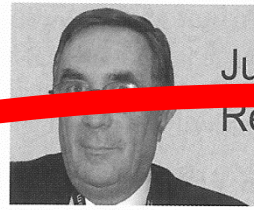
IMPROVE TRIAL

WIDELY QUOTED ON INTERNET &
IN VASCULAR NEWS AS SHOWING:

"NO DIFFERENCE BETWEEN ENDOVASC & OPEN REPAIR" !!!

vascularNEWS
INTERNATIONAL
Issue 61 January 2014

Piergiorgio Cao: Hybrid arch repair
Page 14



Juan Parodi: Renal denervation
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Andrew Holden: Profile
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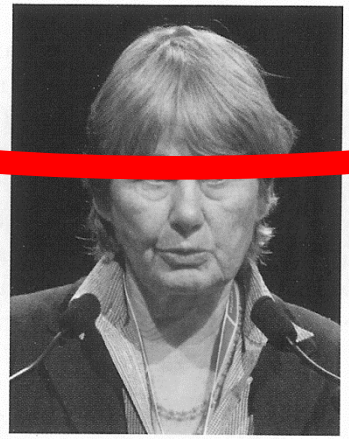
IMPROVE TRIAL 30-DAY RESULTS

No difference between endovascular and open repair for ruptured aneurysms

Thirty-day mortality results from the IMPROVE trial show no difference between an endovascular strategy and open repair in the treatment of ruptured abdominal aortic aneurysms. In the study, the endovascular strategy arm had an overall mortality rate of 35% against 37% in the open repair arm. The results also indicate that open repair patients seen out-of-hours had higher mortality than those seen in-hours, blood pressure control has an important role on outcomes, and EVAR shows better results when patients are treated under local anaesthesia



arm, if they were not suitable, they would have open repair as part of the protocol. "We also anticipated that some of the patients would end up with a final diagnosis that was not aneurysm related," said Powell.

The trial team—Powell, Pinar Ulug, Rob Hinchliffe, Michael Sweeting, Manuel Gomes, Matt Thompson and Roger Greenhalgh—present-

went urgent CT scan and had EVAR if this modality was possible; if not, they had open repair. In the open repair arm, CT scan was optional. A CT scan was performed in 97% of patients in the endovascular strategy group and 90% in the open repair group.

The baseline characteristics were similar for both groups. When comparing the endovascular strategy with the

IMPROVE TRIAL

RDMIZD 316 PTS TO ENDOVASC STRATEGY & 297 TO OPEN REPAIR

30-DAY MORTALITY

EV STRAT GROUP – 35%

OPEN REP GROUP - 37%

NO SIGNIGICANT DIFFERENCE

BUT MUST SEE DETAILS !!!

IMPROVE DETAILED RESULTS

OF 316 PTS RANDOMIZED TO ENDOVASCULAR STRATEGY

154 HAD EVAR: Mortality – 27%

112 HAD OP REP: Mortality – 38%

OF PTS RANDOMIZED TO OPEN REPAIR

36 HAD EVAR: MORTALITY 22%

220 HAD OP REPAIR: MORTALITY 37%

WHEN THE 2 GROUPS WERE COMBINED

MORTALITY OF ALL PTS

TREATED BY EVAR = 25%

MORTALITY OF ALL PTS

TREATED BY OPN REP = 38%

WHICH Rx DO YOU THINK IS BETTER?

EVAR OR OPEN REPAIR ?

TO ME IT SEEMS THAT THE

IMPROVE TRIAL

CLEARLY SHOWS THAT EVAR IS THE BETTER TREATMENT FOR RAAA PATIENTS

- IF IT CAN BE DONE

WHAT ABOUT GUIDELINES ?

SPECIFICALLY CAROTID GUIDELINES

PURPOSE OF GUIDELINES

WHEN Rx OF A MEDICAL CONDITION IS COMPLEX, GUIDELINES SUMMARIZE CURRENT KNOWLEDGE TO OPTIMIZE PATIENT MANAGEMENT & OUTCOMES

PROBLEM: WHO WRITES THE GUIDELINES & THEIR POTENTIAL FOR BIAS

SO LET'S LOOK AT THE GUIDELINES FOR ASX & SX CAROTID STENOSIS (ACS & SCS)

ABBOTT ET AL: STROKE 2015;46:3288-3301
SYSTEMATIC REVIEW OF
CAROTID GUIDELINES

VEITH & BELL: EUR J VASC ENDOVASC SURG
2016;51:471-472
COMMENTARY ON GUIDELINES
& ABBOTT'S REVIEW

ABBOTT ET AL REVIEWED
34 CAROTID GUIDELINES
FROM 23 COUNTRIES
IN 6 LANGUAGES
FROM 32 WRITING GROUPS
DID THEY ALL AGREE?

NO !

THIS DESPITE FACT THAT 34 GUIDELINES WERE BASED ON PRECISELY THE SAME TRIALS, RCTS & DATA!!!

READ THE ARTICLES

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SOME STRIKING EXAMPLES OF DISCREPANCIES & FLAWS

- CAS FOR AVERAGE RISK ACS ENDORSED BY 63% OF GUIDELINES WHILE 30% OPPOSED IT
- CAS FOR AVERAGE RISK SCS ENDORSED BY 50% GLs WHILE 25% OPPOSED IT

REMEMBER ALL 34 GUIDELINES WERE BASED ON PRECISELY THE SAME TRIALS, RCTS & DATA!!!

MORE STRIKING EXAMPLES OF FLAWS IN THESE GUIDELINES

- ENDORSEMENTS OF CAS FOR ACS & SCS DESPITE NO RCT PROOF OF EQUALITY IN STROKE PREVENTION WITH CEA OR BMT

- RCT AND REGISTRY DATA FOR STROKE RISK OF CAS IGNORED IN MANY GUIDELINES

MORE STRIKING EXAMPLES OF FLAWS IN THESE GUIDELINES

- CAS ENDORSED FOR PTS AT HI RISK FOR CEA (BECAUSE OF ANATOMY, MEDICAL DIS, ???) IN 84% OF GLs FOR SCS & 49% OF ACS - DESPITE LMTED LIFE EXPECT OF MANY PTS & NO RCT DATA vs MEDICAL Rx
- NO RECOMMENDATIONS FOR MED Rx IN 32% OF GLs FOR ACS & 9% OF GLS FOR SCS !
- NO RECOMM FOR PERI-PROC MED Rx IN 50% - 52% OF CAROTID GUIDELINES !

MORE STRIKING EXAMPLES OF WEAKNESSES & FLAWS IN GLs

- ALL 34 GLs BASED ON RCTs OF CEA vs BMT FROM 12-34 YEAR OLD TRIALS!!!
- IMPROVED MEDICAL Rxs & BETTER PATIENT SELECTION TOTALLY IGNORED IN MOST OF THE GUIDELINES
- RCTs OVERWEIGHTED IN ALL GUIDELINES
- DEGREE OF CAROTID STENOSIS & TARGET PT POPULATION NOT DEFINED IN >80% OF GLs

MORE STRIKING EXAMPLES OF WEAKNESSES & FLAWS IN GLs

- THESE LACK OF DEFINITIONS & FAILURE TO SPELL OUT LIMITATIONS ALL PROMOTE OVERUSE OF PROCEDURES

- SUMMARY: GLs HAVE FACTUAL ERRORS, INCONSISTENCY, DOCTOR & SPECIALTY BIAS & SELF-INTEREST !!!

REMEDIES FOR FUTURE GUIDELINES

- ELIMINATE DR AND SPECIALTY BIAS & SELF-INTEREST; OBJECTIVE WRITING GROUPS OR OVERSIGHT- NOT EASY
- AVOID OVER-RELIANCE ON RCTs; ACCEPT NEW NON-RCT EVIDENCE
- ACKNOWLEDGE LIMITATIONS GLs
- ACCEPT SOME INCONSISTENCY WITH GLs IN DIFFERENT LOCATIONS WITH DIFFEREENT HABITS & RESOURCES

CONCLUSION & TAKE HOME MESSAGE

- BE AWARE OF THE FLAWS & LIMITATIONS IN GUIDELINES & RCTs
- THEY ARE NOT THE HOLY GRAIL THEY ARE CLAIMED TO BE
- USE THEM APPROPRIATELY & WITH THESE POINTS IN MIND IN YOUR PRACTICE DECISIONS


THANKS FOR YOUR
ATTENTION
HOPEFULLY DISCUSSION