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Research Article

Second Arterial Graft: Right Internal Mammary Artery and Radial Artery. Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Received: February 03, 2019; **Published:** May 27, 2019

Abstract

Background: Conventional approach for coronary artery bypass grafting (CABG) with left internal mammary artery (LIMA) and saphenous vein grafts (SVG) for the last decades seemed reasonable option in patients with multi-vessel coronary artery disease (CAD). However, unfavorable long-term patency of SVG gives the clue to use more arterial grafts. The aim of this study is to assess Randomized Controlled trials (RCT) data in the field of second arterial graft: Right internal mammary artery (RIMA) and Radial artery (RA).

Methods: A systematic review and meta-analysis was made according with the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

The primary outcomes were the following:

1) Angiographic patency for RA vs SVG
2) Any cause of death for bilateral internal mammary arteries BIMA-LIMA groups.

Medline, Cochrane library and Embase were screened and analyzed by first and second investigator. Also, additional sources of data were used to lower publication bias. Last search was performed on March 3, 2019. Meta-analyses was calculated for only RCT with as long as possible follow-up, but not less than 2 years. Authors assess Risk Ratio as intuitive, simple-to-interpret measure. Random-effect model is used in case of heterogeneity, otherwise - fixed effect model used. Binary events have been combined with Inverse Variance method by Review Manager 5.

Results: For 5 RCT with total population of 5274 patients, Systematic review and Meta-analysis was performed.

RA vs SVG: 3 RCT with 5, 7.7 and 10 year follow-up, 1322 patients.

Angiographic patency was significant higher in RA arm compared to SVG (Risk ratio 0.55; 95% CI 0.35 - 0.86; I^2 = 8%).

BIMA(Multi-Arterial) vs LIMA(Single-Arterial): 2 RCT with 2 and 10 year follow-up, 3952 patients.

In not-adjusted data (only BIMA vs LIMA) - All causes death did not achieved statistically significant difference between two groups (Risk ratio 0.93; 95% CI 0.75 - 1.15; I^2 = 10%).

Adjusted data for our research question comparing Multi-Arterial vs Single - arterial strategy showed next: All causes of death statistically significant favor Multi-Arterial arm (Risk ratio 0.80; 95% CI 0.70 - 0.92; I^2 = 0%). More on our adjustment in correspondent section.

Conclusions: In present meta-analysis we assessed 5 RCT studies and population of 5274 patients. We looked on this RCT from the multi-arterial point of view, be aware of this.

Shown statistically significant angiographic superiority of using a RA over SVG. Surveillance data from all causes of death in BIMA (LIMA+RIMA) compared to LIMA+SVG/RA group didn't show superiority. In contrast, adjusted from multi-arterial point of view statistical results (Multi-Arterial vs Single-Arterial) favour Multi-arterial arm. Although these findings may differ from some official conclusion of included studies, in discussion section we had been figured out reasons for that. On the other hand, these results coincided with numerous meta-analysis of huge observational studies.

Emphasize on the need to utilize the second arterial graft (RA or BIMA or other) according to indications for arterial grafting. We emphasize on benefits for patients in terms of long -term patency as well as all causes surveillance. To assess our hypotheses ROMA trial results are awaited. Additional RCT data are of crucial importance.

Keywords: *Coronary Artery Bypass Grafting (CABG); Left Internal Mammary Artery (LIMA); Saphenous Vein Grafts (SVG); Coronary Artery Disease (CAD)*

Abbreviations

CABG: Coronary Artery Bypass Grafting Surgery; RCT: Randomized Controlled Trial; CAD: Coronary Artery Disease; LIMA (LITA): Left Internal Mammary (Thoracic) Artery; RIMA (RITA): Right Internal Mammary (Thoracic) Artery; BIMA (BITA): Bilateral Internal Mammary (Thoracic) Artery = LIMA+RIMA; RA: Radial Artery; SVG: Saphenous Vein Graft; Multi-Arterial: Multi-Arterial Graft Revascularization; Single-arterial: Single-Arterial Graft Revascularization (LIMA graft + SV); DSWI: Deep Sternal Wound Infection; RR: Risk Ratio; HR: Hazard Ratio; CI: Confidence Interval

Introduction

Nowadays, CABG surgery is the most common cardiosurgical operation as well as one of the most common major surgical operations. In US in 2016 only isolated CABG acounts 54% (156,931) of More Commonly Performed Cardiac Surgical Procedures [1] (Figure 1).

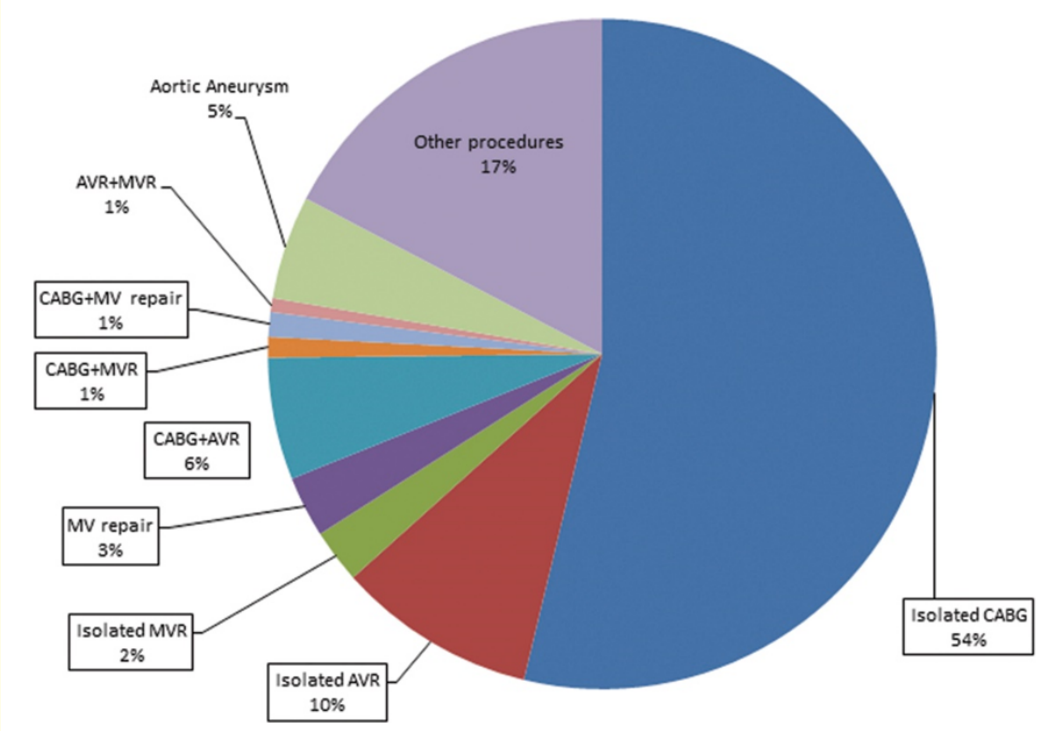

Figure 1: *Relative proportion of cardiosurgical operations by procedure type (2016 year, USA).*

In this review we raised a question about clinical advantage of using second, additional, arterial graft (RIMA and/or RA) during CABG.

Note: We want to put emphasis that when we are talking about RIMA or BIMA we are meaning actually the same. In this article we mean that RIMA used as an additional arterial graft to LIMA. We don't talk in this review about cases when RIMA used instead of LIMA in Single-arterial CABG operations.

One of the reason, to make this review was the comment, which was given by Professor D. Taggart, Chief Investigator and Professor of

Cardiac Surgery at the University of Oxford, UK: "ART [study-author] is one the largest trials with the longest duration of follow-up ever undertaken in cardiac surgery to guide future practice with regards to conduit selection for CABG. While the trial did not show that using two internal thoracic arteries is superior to one, it raises the possibility that any two arterial grafts (internal thoracic or radial) may provide better outcomes than a single [arterial - author] graft for patients undergoing CABG surgery" [2].

As become clear from this quote of professor Taggart, actually there are modest number of operations worldwide, which use a BIMA and/or RA. Although benefits of Multi-Arterial grafting and especially its superiority in long-terms outcomes were discussed in scientific and practical community [3,4].

According to the report of The Society of Thoracic Surgeons, in US at 2016 BIMA and RA has been used in about 5 - 6% off-pump CABG operations each. Using of BIMA is quite stable across last decade, while using of RA actually decreased over time (Figure 2).

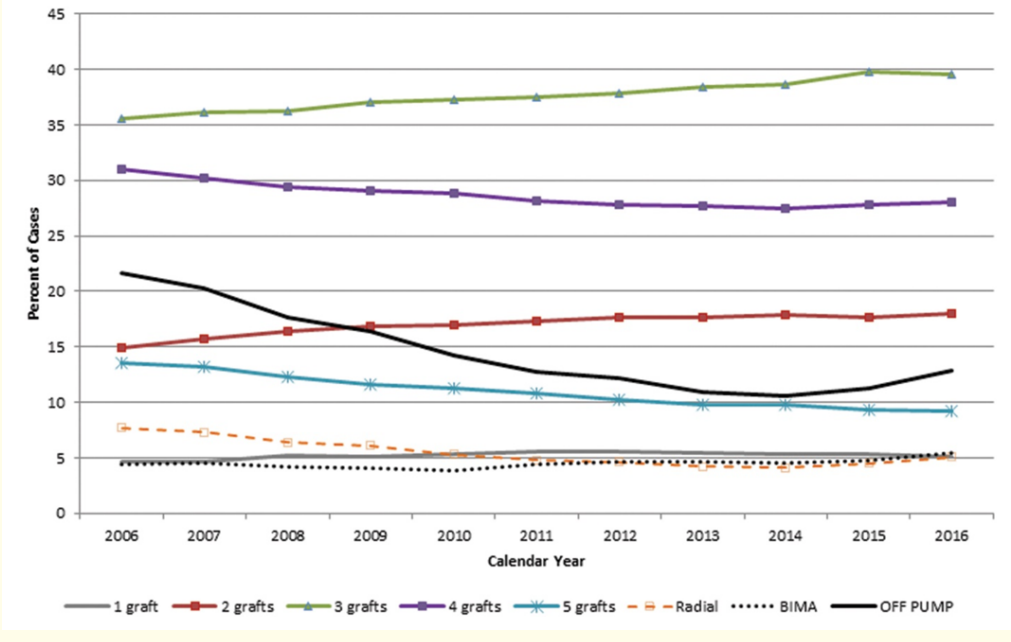

Figure 2: *Coronary artery bypass grafting: US trends in type of grafts for off-pump CABG procedures from 2006 to 2016 [5].*

According to Tatoulis., *et al.* data, BIMA usage in UK and Australia accounts about 10% [5].

Aim of the Study

The aim of our study is to assess Randomized Controlled trials (RCT) data in the field of second arterial graft - Right internal mammary artery (RIMA) and Radial artery (RA) vs saphenous vein graft (GSV).

Materials and Methods

A systematic review and meta-analysis was made according to the Cochrane Handbook for systematic reviews of intervention and preferred reporting item for systematic reviews and meta-analysis (PRISMA) statement [6,7].

Medline, Cochrane library and Embase were screened. Additional sources as professional journals, sites of professional organizations, scientific conference theses and press releases etc. were used for decreasing publications bias. Snow-bolling technique and

cross-searching of related/similar + citing articles were made. We reviewed abstracts of all articles and of "related articles" and references of reviews. Scientific networking as a source has been used. Unpublished RCT results have been also reviewed. Last search was made on March 3, 2019.

Search terms for different bases were relevant MeSh and EmTree terms, Cochrane terms. Some examples of search words: "CABGS" thoracic, "CABGS" radial, "radial artery coronary bypass" , "radial artery patency", "radial artery harvest*", "radial artery graft, "randomized controlled trial" [Publication Type]), "meta analysis" [Publication Type]), "guideline" [Publication Type], "systematic review" [Publication Type], "coronary artery disease/surgery" [MeSH Terms], "follow up studies" [MeSH Terms], "coronary artery bypass" [MeSH Major Topic], Humans [Mesh], arteries" [MeSH Terms], arter*" [All Fields], revascularization [All Fields]); Coronary Disease/surgery*, Arteries/transplantation*, Radial Artery/diagnostic imaging, Radial Artery/transplantation, Thoracic Arteries/diagnostic imaging, Thoracic Arteries/transplantation, Mammary Arteries/transplantation, Saphenous Vein/transplantation*, Mammary Arteries/surgery* etc.

We planned to include only RCT with as long as possible follow- up, but not less than 2 years. Reasons are next: observational studies shown that arterial grafts have benefit in long term follow-up compare to SVG [3,8].

In short term SVG works fine and vein graft failure is rare. Also in short term - crucial role play technical mistakes which both grafts prone to.

The primary outcomes were:

1) Angiographic patency for RA vs SVG.
2) Death from any cause for BIMA vs Single-arterial groups.

Graft failure has been characterized as: functional and complete graft occlusion (TIMI flow grade 0 or 1 or 2), angiographic string sign, complete occlusion. Death from any cause was used to avoid benefits of Multi-Arterial grafting and especially its superiority in long-terms outcomes misunderstandings in terms from study to study, as it is known issue in Cardio-Thoracic surgery.

Authors aware of comparing apples and oranges [9] and would be thankful for constructive critics of our work.

All data have been analyzed by investigator (MA) and then reviewed and edited by second investigator (SY). Threshold for selecting abstracts for full-text review was low. Main and relevant data were extracted from full-text articles. Disagreement about inclusion or exclusion of the studies have been solved by group discussions and finding consensus. Unpublished data of 10 year follow-up of RAPCO trial by Hayward., *et. al.* (2016) extracted from authors Conference abstract at AATS ANNUAL MEETING 2016 in Baltimore US.

Statistical software for our review was Review Manager 5. Authors assess Risk Ratio with 95% confidence interval (CI) as intuitive, simpler-to-interpret measure.

Random-effect model has been used in case of heterogeneity, otherwise-Fixed effect model. Binary events have been combined with Inverse Variance method by Review Manager 5.3.

Risk of bias have been assessed using 3 level schemes used in Cochrane Review Manager - unclear, low and high risk.

For classification of heterogeneity - I^2 statistics was used. Low, moderate, substantial, and considerable heterogeneity were equal to value of I^2 0 - 40, 30 - 60, 50 - 90 and 75 - 100% sequentially. Funnel plot analysis for publication bias will be performed for 10 and more included studies. Summarized quality of evidence assesses using four level schemas: high, moderate, low and very low. For example in GRADE, observational studies start from low level and RCT data starts from high. Level can be upgraded in case of large magnitude of effects (RR > 2 or < 0.5) etc. or downgraded in case of small study population, using partly unrandomized data or extracting unmasked existed data for different research question than initially was in RCT etc [10,11].

Results

We have identified 2113+52 = 2165 articles after duplicates removal (Figure 3). All articles have been screened and 165 abstracts reviewed, as a result, 117 have been excluded.

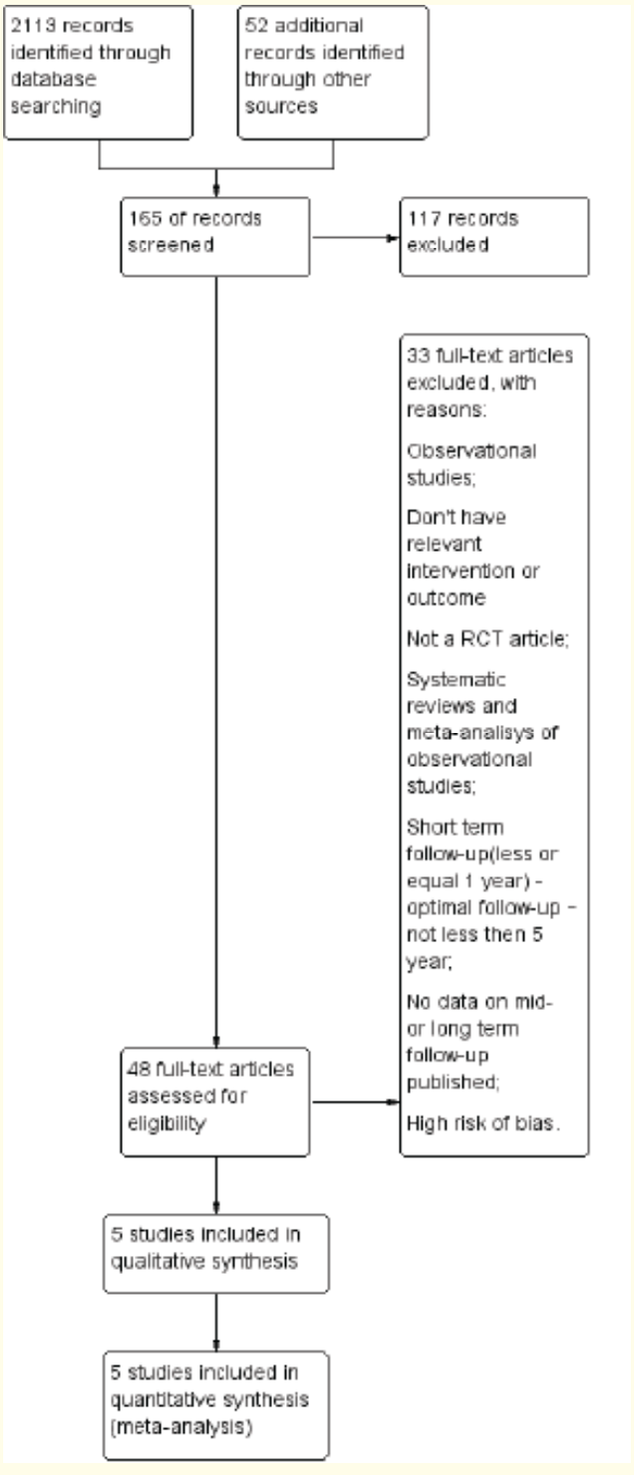

Figure 3: *PRISMA study flow diagram.*

Totally 48 full-text articles have been studied. Observational studies have been excluded. The qualitative synthesis was made for 5 RCT, which have met inclusion criteria. General risk of bias was assessed and graded as low. Study characteristics represented in table 1.

Study	Study design	Population	Sample size	Years of study	Follow-up time (years)	Last follow-up Data (year)
First group (RA)						
RSVP Collins	A prospective, single-center, randomized clinical trial	1 center in the United Kingdom	142	1998 - 2000	5	2008
RAPS Deb	A prospective, multicenter randomized clinical trial	12 university Canadian centers and 1 from New Zealand	561	1996 - 2001	7.7	2012
RAPCO Hayward	Single-center, open label, 2 tiered randomized controlled trial	1 center in Australia	619	1996 - 2004	10	2016
Second group (RIMA)						
Stand-in-Y Nasso	A prospective, randomized clinical trial	Italy	803	2003 - 2006	2	2009
ART Taggart	Two-group, multicenter, randomized, unblinded trial	28 hospitals in seven countries: Australia, Austria, Brazil, India, Italy, Poland, and the United Kingdom)	3102	2004 - 2007	10	2019

Table 1: *Study characteristics of included RCT. RSVP: Radial Artery versus Saphenous Vein Patency trial [14]; RAPS: Radial Artery Patency Study [15]; RAPCO: Radial Artery Patency and Clinical Outcomes study [16]; Stand-in-Y: Stand-in-Y Mammary Study [17]; ART: Arterial Revascularization Trial [18].*

All 5 RCT have been comparing LIMA + second arterial graft (RA or RIMA) with conventional schema LIMA + SVG at follow-up of 5, 7,7, 10, 2 and 10 years. Just to remind, our research question was focused on the best second isolated graft for CABG. To avoid biases, for qualitative synthesis we have decided to divide studies in two groups.

First group was mainly focused on comparison of RA vs SVG.

Second group was mainly focused on BIMA vs LIMA. For second group, two different qualitative analysis was made. Main reason was ART study data and difference, which bring to it - comparison of Multi-arterial graft vs Single-Arterial graft strategy. More on that, in section about qualitative synthesis of second group.

The first group consist of 3 RCT [12-14].

Qualitative analysis for angiographic patency of RA vs SVG was made. Unfortunately, survival data could not been extracted from all 3 studies. Meta-analysis showed that graft failure occurred in 8,8% (35/397) in RA and in 16,5 % (64/388) in SVG arms. Data were consistent in all 3 studies. This indicates that RA angiographic patency significantly higher at 5 to 10 years follow-up than in SVG: Risk Ratio (RR) 0.56, 95 % CI 0.38 - 0.83, P = 0.004, I^2 = 8% (Figure 4).

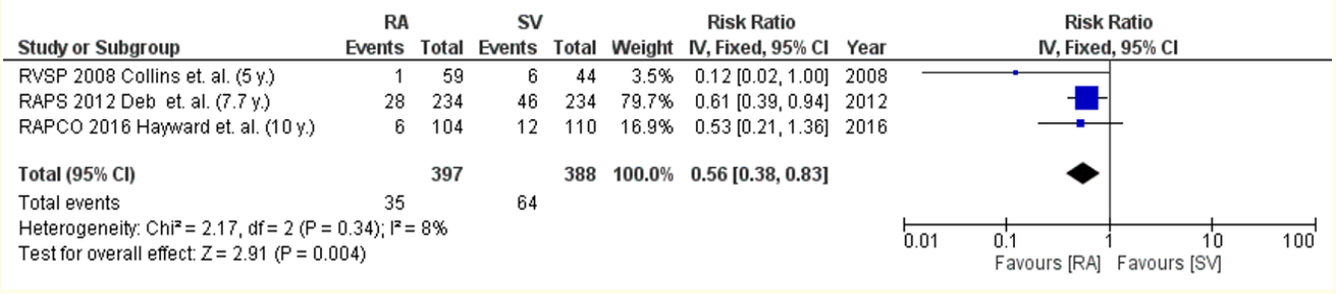

Figure 4: *Forest plot of angiographic patency RA vs SVG.*

Whether RA angiographic superiority over SVG transforms at survival superiority is unclear. RAPCO trial [15] of modest population with 10 year follow-up data (unpublished) in 2016 conclude that it didn't influence survival.

Before we move to the second group, at RAPCO 2016 was also represented comparison of RA vs RIMA for All cause death and for angiographic patency. In graphic form, you can find it at figure 5. Authors conclude that in younger patients RA have a patency rate equivalent to RIMA, but have superior survival. For RAPCO author reasons of this fact are unclear [14].

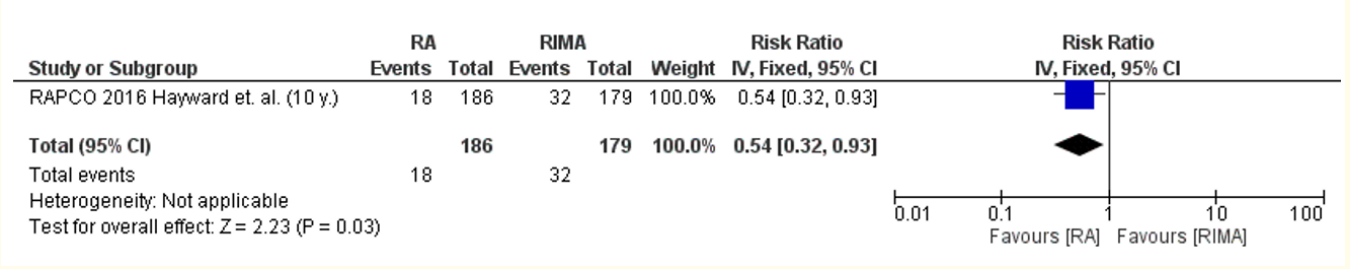

Figure 5: *Data form RAPCO 2016 (unpublished) of All cause death RA vs RIMA for younger patients.*

The Second group consists of 2 RCT. Random-effect model was used. In Stand-in-Y modest population size study follow-up was 2 year and ART has 10 year follow-up data.

The Stand-in-Y Mammary trial 2009 Nasso., *et al.* (2 y.) studied 850 patients randomly assigned to 4 groups, three of them Multi-arterial and one was Single-Arterial: two BIMA groups with different methodic, one LIMA + RA and opposite one LIMA + SVG group. At follow-up of only 24.1 ± 9.8 months, was found no difference in survival between the groups (Odds ratio 0.63, 95% CI 0.27-1.47, *P* = 0.62) [15].

The Arterial Revascularization Trial (ART) assessed 3102 randomized patients to whether BIMA (*n* = 1548) or a SIMA (*n* = 1554) group. The primary outcome was overall survival at 10 years.

Intention-to-treat analysis demonstrate 315 (20.3%) and 329 (21.2%) deaths in the BIMA and SIMA groups respectively (hazard ratio 0.96; 95% CI 0.82 - 1.12, P = 0.62). No significant difference was between two groups in All cause deaths at 10 years [16].

As mentioned before, we have made two separate Meta-analysis in this group.

One with original data, non-adjusted for our research question and second with adjusted data. The reason for this was ART study, as the most robust RCT in our study [16].

The idea of ART study was comparing LIMA vs BIMA. But 13.9% of randomly assigned to BIMA arm has a LIMA + SVG grafting. In LIMA arm 21.8% of patients have gained second arterial graft (RA) and study design ignore impact of RA. ART authors explain that in 2001, when study designed wasn't known of beneficial RA clinical impact. The question of ART are LIMA vs BIMA, ignoring RA, but ART study posted also data for research question such as CABG operations with only "One arterial graft" vs "Two or more arterial graft". This data we extract in ART for second "adjusted" Meta-analysis in this group (Figure 7).

Be aware, extracting this data and including in the second Meta-analysis can be conjugated with biases, they are not randomized/unmasked actually, thus can downgrade the quality of evidence.

Not-adjusted group represent data from ART study as "intention-to-treat" (Figure 6). This mean all patients randomized to BIMA or LIMA + SVG remains there irrespectively of actual treatment. It worth mentioned that in as "per-protocol" ART analysis results were same. "Per-protocol" means that each groups contains only patients who get surgery according to their randomized assignment, no crossover data. No significant differences were between BIMA and SIMA in All cause death at 10 years follow-up. Significant higher prevalence of

sternal wound complications occurred in 54 (3.5%) in the BIMA and in 30 patients (1.9%) in LIMA group at 6 month follow-up (relative risk 1.81; 95% CI 1.16 - 2.81) [16].

Summarized non-adjusted data represented at figure 6. No significant difference in all cause death of BIMA vs LIMA was shown (RR 0.93, 95 % CI 0.75-1.15, P = 0.51, I^2 = 10%).

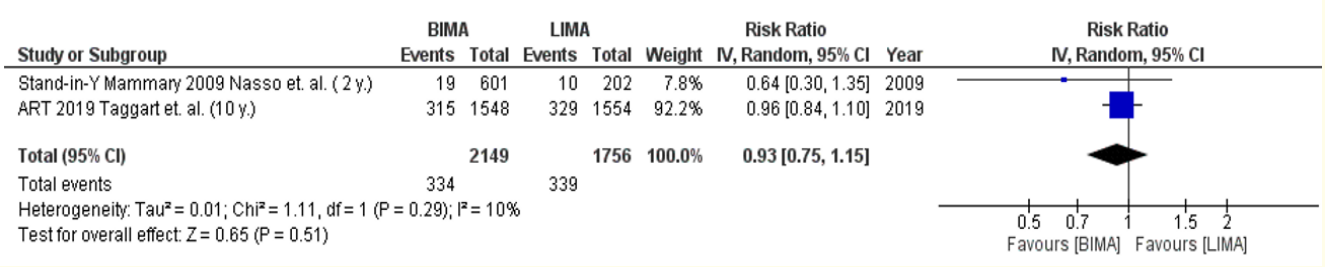

Figure 6: *Forest plot of All cause death BIMA vs LIMA (not-adjusted, higher quality of evidence).*

Figure 7 represent meta-analysis with adjustment of ART data for Multi-Arterial methodic (LIMA + RIMA and/or RA + SV) vs Single-Arterial (LIMA+SV).

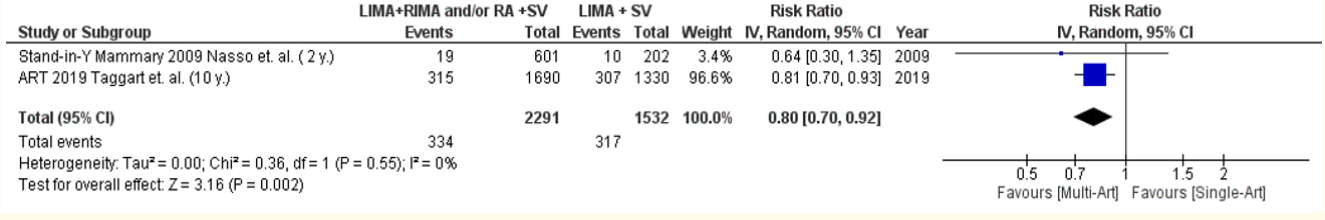

Figure 7: *Forest plot of All cause death Multi-Arterial vs Single-Arterial (LIMA) grafting (adjusted, lower quality of evidence).*

Data was gained from original ART study publication of 10-y follow-up (2019) [16]. Date for [Multi-Arterial] group we get with summation of columns Yes-RA in "Single graft" group and both Yes-RA and No-RA for "Bilateral graft" group. For [Single-arterial] group we take only No-RA in "Single graft".

It significantly favours Multi-arterial arm over Single-Arterial (RR 0.80, 95% CI 0.70-0.92, P = 0.002, I^2 = 0%).

As this meta-analysis included only 3 and 2 studies, we did not perform funnel plot analysis. Evidence of publication bias exist, but we extracted unpublished data of 10 year follow-up of RAPCO trial by Hayward., *et al.* (2016) from authors Conference abstract at AATS ANNUAL MEETING 2016 in Baltimore US and so discharge this risk. Inconsistency in data was not supposed to be serious as heterogeneity was low (not more than I^2 = 10).

Summarized quality of evidence assessed with serious prejudgment to downgrading. We use only RCT data from proved centers so it can be initially graded with high [11].

Upgrading criteria as large magnitude of effects wasn't observed (RR > 2 or < 0.5) on the other hand study populations were modest, included some studies with shorter follow-up time and for ADJUSTED meta-analysis extracted partly unrandomized/unmasked existed data for different research question than was initially in RCT etc. To sum it up, using four level schemas it was graded as moderate.

Discussions

We focus only on a RCT data in our Systematic review as the top pin of Evidence based medicine. As a result we get a very modest patients population, compared to other studies. Including an observational studies allow us to get far bigger population, but our aim was getting the best quality RCT for meta-analysis and so increase quality of evidence.

Data from histo-pathological studies shown that atherosclerosis development rate for LIMA and RA are quite low (0,7% and 5.3% respectively) in contrast to SVG. RIMA histologically quite similar to LIMA. They are not so disposed to endothelium hyperplasia as SVG as well. More on histology and comparing of RA, LIMA and SVG you can find in work of Rehman., *et al* [18].

So, it seems logic, that additional arterial graft should bring benefit compared to conventional SV strategy.

But in introduction section we mention that use of the RIMA/BIMA are rather low as well as RA. The reasons are unclear but we can propose several: longer time of operation, increased complexity and unfamiliarity of surgeons with the techniques, lack of RCT data and prejudgment about vulnerability to deep sternal wound infection in case of BIMA.

Analysis of radial artery as a conduit

Our systematic review and Meta-analysis have shown that RA angiographic patency significantly higher at 5 to 10 years follow-up than in SV (RR 0.56, 95 % CI 0.38 - 0.83, P = 0.004, I^2 = 8%). This RCT evidence support existing observational studies and literature data [8,19].

But whether RA angiographic superiority over SVG transforms at superiority in survival is unclear. RAPCO trial of modest population with 10 year follow-up data (unpublished) in 2016 conclude that for older patients it didn't influence survival. That mean additional RCT have to be performed.

2018 ESC/EACTS Guidelines on myocardial revascularization [20] recommend using RA over SVG in high-grade stenosis (IB). RA should be used in > 70% and ideally > 90% stenosis [21]. Also, Guidelines mention three studies and declare that radial artery as the second conduit correspond with increased survival in registry studies [22-24].

The ROMA trial-rationale and study protocol aggregate matched observational studies with each more than 1000 patients and follow-up more than 3 years. They include next studies: Cohen., *et al.* 2001 (1434 patients), Tranbaugh., *et al.* 2010 (4271 p.), Locker., *et al.* 2013 (8622 patients), Schwann., *et al.* 2015 (11 261 patients), Shi., *et al.* 2016 (4006 patients). Authors of ROMA summarize that All of this studies consistent over fact, that RA have a moderate survival benefit over SVG [25].

About RA configuration (aorto-coronary or composite) it looks like both are safe. Sequential anastomoses may raise patency over single anastomosis [18].

RAPCO 2016 was also represented comparison of RA vs RIMA for All cause death and for angiographic patency. Authors conclude that in younger patients RA have a patency rate equivalent to RIMA, but have superior survival. For RAPCO author reasons of this mechanism is unclear [14].

RIMA conduit analysis

Generally, RA meta-analytic data correspond with existing literature. But analyzed data about RIMA actually surprised us, especially 2019 data of 10 year follow-up of ART study. It has to be a very robust source of evidence regarding BIMA grafting. But in conclusion of 10 years follow-up it has failed to show superiority of BIMA over LIMA in all cause death and higher prevalence of DSWI in BIMA arm. In contrast many observational studies have shown superiority of BIMA over Single-arterial graft strategy [3,26-30].

Of 'course, be aware, strongly influenced results limitation of this study and its design made back in 2001. The first one - is data it was based on - it was mostly 1980s and the 1990s data, when rate of adverse and lethal events were much higher. Also, authors of ART confess that back then in 2001 were no data of clinical RA benefit and so almost quarter of LIMA group get additional arterial graft in form of RA. Hence in 21.8% of patients the ART compare BIMA vs LIMA+RA instead of BIMA vs LIMA+SVG.

The third one, actual treatment of randomized patients and crossover: in BIMA arm 83.6% get BIMA grafts, and in LIMA arm - 96.1% patients get allocated treatment. It is a high rate of crossover-13.9% of randomized patients instead of BIMA received only a single internal thoracic artery graft [16].

As for BIMA indication, Kieser., *et al.* recommend consider BIMA grafting in younger than 69.9 years patients [31].

Same idea have 2018 ESC/EACTS Guidelines on myocardial revascularization and recommend to "consider in patients with a reasonable life expectancy and a low risk of sternal wound complications" BIMA grafting [20].

DSWI and its higher prevalence in BIMA group are a serious concern. To deal with it, for example Nau., *et al.* skeletonized BIMA technique and emphasize on greatest benefit in men and patients with chronic obstructive pulmonary disease [32].

2018 ESC/EACTS Guidelines on myocardial revascularization also suggest that although higher potential risk of mammary injury it has a lot of benefit such a longer conduit, higher agility, higher blood flow, and fewer wound-healing problems [33-39]. Consequently, guidelines recommend skeletonized technique in patients with higher risk of sternal wound complications.

Our research team hopes this study will help to find gaps in evidence. There are strong needs in large RCT trials, which will compare the best practice of RIMA, RA utilization and compare long term clinical and angiographic patency results. Moreover, it looks logic to invest more time in comparing different arterial grafts for different cases and less time for saphenous vein grafts. We actually have question about the very best second graft, arterial graft, but it looks solid that vein graft are not the best one. Investment in standardization in the field of second arterial graft brings promise to a profitable result for public health.

Awaiting for the results from the ROMA trial which aim to compare clinical outcome of single versus multiple arterial grafts. Additional RCT in this field are required.

Conclusion

In current study we assessed 5 RCT studies and population of 5274 patients. We looked on this RCT from the multi-arterial point of view, please be aware of that.

Statistically significant angiographic superiority of utilizing a RA over SVG were achieved. Surveillance data from all causes of death in BIMA (LIMA+RIMA) compared to LIMA+SVG/RA group did not show superiority. In contrast, adjusted from multi-arterial point of view statistical results (Multi-Arterial vs Single-Arterial) favor Multi-arterial arm. Although these findings may differ from some official conclusion of included studies, in discussion section we had been figured out reasons for that. On the other hand, this results coincided with numerous meta-analysis of huge observational studies.

Emphasize on the need to utilize the second arterial graft (RA or BIMA or other) according to indications for arterial grafting. We emphasize on benefits for patients in terms of long-term patency. To assess hypothesis ROMA trial results are awaited. Additional RCT data are of crucial importance.

Conflict of interest

The authors declared no conflict of interest with respect to this manuscript.

Bibliography

1. D'Agostino RS., *et al*. "The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2018 Update on Outcomes and Quality". *Annals of Thoracic Surgery* 105.1 (2018): 15-23.

2. "Ten-year outcomes of the Arterial Revascularisation Trial revealed today". Taggart. Munich, Germany (2018).

3. Buttar SN., *et al*. "Long-term and short-term outcomes of using bilateral internal mammary artery grafting versus left internal mammary artery grafting: a meta-analysis". *Heart* 103.18 (2017): 1419-1426.

4. Squiers John J and Michael J Mack. "Coronary artery bypass grafting-fifty years of quality initiatives since Favaloro". *Annals of Cardiothoracic Surgery* 7.4 (2018): 516-520.

5. Tatoulis J., *et al*. "The right internal thoracic artery: is it underutilized?" *Current Opinion in Cardiology* 26.6 (2011): 528-535.

6. Higgins JPT and Green S. "Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]". The Cochrane Collaboration (2011).

7. Moher D., *et al*. "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement". *International Journal of Surgery* 8.5 (2010): 336-341.

8. Benedetto U., *et al*. "Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trials†". *European Journal of Cardio-Thoracic Surgery* 47.1 (2015): 59-65.

9. Barone JE. "Comparing apples and oranges: a randomised prospective study". *British Medical Journal (Clinical Research Ed.)* 321.7276 (2000): 1569-1570.

10. Guyatt Gordon H., *et al*. "What is "quality of evidence" and why is it important to clinicians?" *British Medical Journal (Clinical Research Ed.)* 336.7651 (2008): 995-998.

11. Atkins D., *et al*. "Grading quality of evidence and strength of recommendations". *British Medical Journal* 328.7454 (2004): 1490-1494.

12. Collins P., *et al*. "Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up". *Circulation* 117.22 (2008): 2859-2864.

13. Deb S., *et al*. "Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: results from RAPS (Radial Artery Patency Study)". *Journal of the American College of Cardiology* 60.1 (2012): 28-35.

14. Õ *Brian F Buxton., *et al*. "10-Year Endpoint of RAPCO Is Reached: Clinical and Angiographic Results of a Randomised Trial of Radial Artery Versus Right Internal Thoracic Artery or Saphenous Vein for the Second Graft". Conference: AATS ANNUAL MEETING 2016, Baltimore, MD, USA (2016).

15. Nasso G., *et al*. "Arterial revascularization in primary coronary artery bypass grafting: direct comparison of 4 strategies-results of the Stand-in-Y Mammary Study". *Journal of Thoracic and Cardiovascular Surgery* 137.5 (2009): 1093-1100.

16. Taggart DP., *et al*. "Bilateral versus Single Internal-Thoracic-Artery Grafts at 10 Years". *New England Journal of Medicine* 380.5 (2019): 437-446.

17. Ruengsakulrach P., *et al*. "Comparative histopathology of radial artery versus internal thoracic artery and risk factors for development of intimal hyperplasia and atherosclerosis". *Circulation* 100.19 (1999): II139-II144.

18. Rehman SM., *et al*. "The radial artery: current concepts on its use in coronary artery revascularization". *Annals of Thoracic Surgery* 96.5 (2013): 1900-1909.

19. Gaudino M., *et al*. "Radial-Artery or Saphenous-Vein Grafts in Coronary-Artery Bypass Surgery". *New England Journal of Medicine* 378.22 (2018): 2069-2077.

20. Neumann FJ., *et al*. "2018 ESC/EACTS Guidelines on myocardial revascularization". *European Heart Journal* 40.2 (2019): 87-165.

21. Hayward PA., *et al*. "Comparable patencies of the radial artery and right internal thoracic artery or saphenous vein beyond 5 years: Results from the Radial Artery Patency and Clinical Outcomes trial". *Journal of Thoracic and Cardiovascular Surgery* 139.1 (2010): 60-67.

22. Schwann TA., *et al*. "Comparison of late coronary artery bypass graft survival effects of radial artery versus saphenous vein grafting in male and female patients". *Annals of Thoracic Surgery* 94.5 (2012): 1485-1491.

23. Tranbaugh RF., *et al*. "Radial artery conduits improve long-term survival after coronary artery bypass grafting". *Annals of Thoracic Surgery* 90.4 (2010): 1165-1172.

24. Tranbaugh RF., *et al*. "Coronary artery bypass grafting using the radial artery: Clinical outcomes, patency, and need for reintervention". *Circulation* 126.11 (2012): S170-S175.

25. Mario Gaudino., *et al*. "Randomized comparison of the clinical outcome of single versus multiple arterial grafts: the ROMA trial-rationale and study protocol". *European Journal of Cardio-Thoracic Surgery* 52.6 (2017): 1031-1040.

26. Taggart DP., *et al*. "Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries". *Lancet* 358.9285 (2001): 870-875.

27. Takagi H., *et al*. "A metaanalysis of adjusted hazard ratios from 20 observational studies of bilateral versus single internal thoracic artery coronary artery bypass grafting". *Journal of Thoracic and Cardiovascular Surgery* 148.4 (2014): 1282-1290.

28. Yi G., *et al*. "Effect of bilateral internal mammary artery grafts on long-term survival: a meta-analysis approach". *Circulation* 130.7 (2014): 539-545.

29. Rizzoli G., *et al*. "Does the use of bilateral internal mammary artery (IMA) grafts provide incremental benefit relative to the use of a single IMA graft? A meta-analysis approach". *European Journal of Cardio-Thoracic Surgery* 22.5 (2002): 781-786.

30. Weiss AJ., *et al*. "A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting". *Annals of Cardiothoracic Surgery* 2.4 (2013): 390-400.

31. Kieser TM., *et al*. "Outcomes associated with bilateral internal thoracic artery grafting: the importance of age". *Annals of Thoracic Surgery* 92.4 (2011): 1269-1276.

32. Ngu JMC., *et al*. "The balance between short-term and long-term outcomes of bilateral internal thoracic artery skeletonization in coronary artery bypass surgery: a propensity-matched cohort study". *European Journal of Cardio-Thoracic Surgery* 54.2 (2018): 260-266.

33. Deo SV., *et al*. "Bilateral internal thoracic artery harvest and deep sternal wound infection in diabetic patients". *Annals of Thoracic Surgery* 95.3 (2013): 862-869.

34. Lytle BW. "Skeletonized internal thoracic artery grafts and wound complications". *Journal of Thoracic and Cardiovascular Surgery* 121.4 (2001): 625-627.

35. Sa MP., *et al*. "Skeletonized versus pedicled internal thoracic artery and risk of sternal wound infection after coronary bypass surgery: Meta-analysis and meta-regression of 4817 patients". *Interactive CardioVascular and Thoracic Surgery* 16.6 (2013): 849-857.

36. Sakic A., *et al*. "Simple adaptations of surgical technique to critically reduce the risk of postoperative sternal complications in patients receiving bilateral internal thoracic arteries". *Interactive CardioVascular and Thoracic Surgery* 17.2 (2013): 378-382.

37. Wendler O., *et al*. "T grafts with the right internal thoracic artery to left internal thoracic artery versus the left internal thoracic artery and radial artery: Flow dynamics in the internal thoracic artery main stem". *Journal of Thoracic and Cardiovascular Surgery* 118.5 (1999): 841-848.

38. Kajimoto K., *et al*. "Coronary artery bypass revascularization using bilateral internal thoracic arteries in diabetic patients: A systematic review and meta-analysis". *Annals of Thoracic Surgery* 99.3 (2015): 1097-1104.

39. Sa MP., *et al*. "Flow capacity of skeletonized versus pedicled internal thoracic artery in coronary artery bypass graft surgery: Systematic review, meta-analysis and metaregression". *European Journal of Cardio-Thoracic Surgery* 48.1 (2015): 25-31.

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