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Recent Management of Abdominal Aortic Aneurysm

Hossam ElDin Hassan El Azzazy, Haitham Mostafa Elmaleh, Mohamed Ismail Mohamed, Mahmoud Ahmed Adel El-Said
Department of General Surgery, Faculty of Medicine, Ain Shams University
Corresponding author: Mahmoud A. Adel El-Said, Mobile: 01007848418;
Email: mahmod.salem101@yahoo.com

ABSTRACT

Background: Abdominal Aortic Aneurysms had always been one of the most serious causes of mortality in the past decades until recently. Thanks to the modern advances in medicine and the technological revolution in Imaging and endograft Industry, treatment of Abdominal Aortic Aneurysms no longer imposes that high mortality risk it previously had. **Objective:** This study aims to review currently available evidence aiming at designing an approach for the management abdominal aortic aneurysm.

Subjects and Methods: We are planning to search Medline, Plumbed, Cochrane databases using the keywords: "management", " abdominal", " aortic", " aneurysm". Any studies published in English with subjects with surgical and endovascular management of abdominal aortic aneurysm will be included up to 1/3/2017. **Results:** The present systematic review confirmed this belief. EVAR patients had a significantly lower 30-day mortality, shorter hospital and ICU stay, less blood loss or blood transfusion requirement, fewer postoperative cardiac and respiratory morbidities, less colonic ischaemia, and fewer overall postoperative problems compared to open repaired aneurysm patients.

Keywords: Open surgical repair - Abdominal aortic aneurysms - Endovascular aortic aneurysm repair - CT angiography.

INTRODUCTION

Abdominal Aortic Aneurysms had always been one of the most serious causes of mortality in the past decades until recently.

Thanks to the modern advances in medicine and the technological revolution in Imaging and endograft Industry, treatment of Abdominal Aortic Aneurysms no longer imposes that high mortality risk it previously had [(1)].

Four randomized controlled trials have now been published comparing EVAR with open surgical repair (OSR); the UK EVAR 1 Trial [(2)], the Dutch DREAM Trial [(3)], the US OVER Trial [(4)] and the French ACE Trial [(5)].

Patients at greatest risk for Abdominal Aortic Aneurysm (AAA) are men who are older than 65 years and have peripheral atherosclerotic vascular disease. A history of smoking often is elicited. Accordingly, in 2005, the US Preventive Services Task Force (USPSTF) recommended Ultrasonography screening in men aged 65-75 years who had ever smoked. As of June 2014, these recommendations were being updated on the basis of evidence from a 2014 study [(6)].

Not all patients with an AAA are suitable for endovascular repair. The most common reasons to reject a patient based on anatomical configurations include Visceral and renal supply, diameter of the proximal neck, angulation and conical nature of the proximal neck as well as calcification and mural thrombosis in it [(7)].

EVAR (Endovascular Abdominal Aortic Aneurysm Repair) is now a commonly available option for a growing population of patients requiring treatment for AAAs. Some advantages of EVAR over traditional open surgery include shorter hospital stays, fewer postoperative complications, and greatly reduced recovery time; the treatment technique may also result in less operative blood loss [(1)]. New devices with fenestrations and branches have increased the number of patients who are good candidates for EVAR, reducing the population of individuals who would otherwise be resigned to "watchful waiting" for their aneurysms. Recent research now demonstrates that EVAR offers reduced mortality rates compared with open repair [(1)]. Aneurysms are defined as focal dilatations at least 50% larger than the expected normal arterial diameter. A practical working definition of an abdominal aortic aneurysm (AAA) is a transverse diameter of 3 cm or greater, and for a common iliac aneurysm, a transverse diameter greater than 1.8 cm, based on average values for normal individuals [(8)].

The relationship of atherosclerosis to aneurysm formation is complex, but it is clear that both aneurysms and obstructive manifestations are often found in the same patient, whereas either the aneurysmal or obstructive manifestation is predominant in others. Specific factors associated with degenerative aneurysms include the presence of metalloproteinases in the media of aneurysm specimens. In addition, there is evidence for a deficit

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of antiproteolytic enzymes that inhibit metalloproteinases, specifically the tissue inhibitor of metalloproteinase-1 ***(9)***.

The prevalence of AAAs in a given population depends on the presence of risk factors associated with AAAs, including older age, male gender, white race, positive family history, smoking, hypertension, hypercholesterolemia, peripheral vascular occlusive disease, and coronary artery disease (CAD) ***(10)***.

AIM OF THE WORK

This study aims to review currently available evidence aiming at reach best approach for management of abdominal aortic aneurysm.

This review will show literature, research and statistical analysis of results concerned with management options of abdominal aortic aneurysm repair.

SUBJECTS AND METHODS

Methodology:

Study Design: A systematic Review of published English literature from their date of inception till May. 2017.

I) Search strategy: **A) Study site (setting): Sources:** Electronic databases: Medline, PubMed. Bibliographies. Hand searches of journals: Online internet search from the electronic database of Medline via PubMed. "Related articles" function will be used to obtain any relevant articles. Additionally, references of the articles included in the analysis will be reviewed for any other citations. **Study Language:** Only published English literature will be included in the study. **Time Frame:** All studies from their inception date till May., 2017 will be included.

B) Search plan: Primary Medline search for key words "surgical", "endovascular", "abdominal", "aortic", "aneurysm", "repair", in various combinations was done. All the primary search studies that came up were screened regarding the title to remove any duplicates.

Then screened the title and abstract to categorize them into 3 groups: 1) Included primary studies. 2) Not sure. 3) Omitted. Screen full text of the "Not Sure" group to decide if they will be included or omitted according to the criteria previously mentioned. Included studies were categorized according to level of evidence and evaluated for quality using a modified Downs and Black scale. This scale was chosen due to its robustness in evaluating non-randomized methodologies, including cohort and case-control studies. The level of evidence was determined for each study, indicating the quality of methodology used in the study.

Levels of evidence were defined using commonly accepted standards in the literature, as follows: Level 1: Randomized controlled trials (RCTs). ***Level 2:*** Prospective or retrospective cohort studies and poor quality RCTs. ***Level 3:*** Case control studies. ***Level 4:*** Case series or observational studies (cross-sectional analysis). ***Level 5:*** Case reports and expert opinion.

Methods of subject recruitment, group assignment, and use of randomization are examples of considerations used in assigning each study's level of evidence.

C) Inclusion / exclusion criteria: ***Criteria for inclusion and exclusion of studies in the review according to the study design: Included studies:*** - Eligible studies include those comparing the surgical management versus endovascular management of abdominal aortic aneurysm. - Study designs include mainly analytic/observational studies and randomized controlled trials. - Well conducted descriptive studies of good quality were included.

Excluded studies: Case reports or case series with less than ***10*** patients. Abstracts, conference presentations, technical notes, letters, comments and expert opinions were excluded. Studies with the most complete results/follow up were selected in cases of duplicate/cumulative results. Because of the difficulty in conducting randomized controlled trial (RCT) in the domain of surgery, all analytic studies and some descriptive studies concerning both open and endovascular techniques in management of abdominal aortic aneurysm were included in this review.

II. Data collection, analysis and appraisal: After screening full text of the included studies, the following data was extracted from each primary study: 1) Study design. Full reference of article including author, year and source. Population description: Number. Criteria for diagnosis. Any secondary diagnosis. Severity of disease. 2) Intervention: Endovascular repair of abdominal aortic aneurysm (EVAR). Surgical management of abdominal aortic aneurysm. Comparative Group (if relevant). Outcomes & Measurement: The primary outcome of interest included: Operative outcomes and Clinical outcomes. Operative outcomes comprised: operation duration, intraoperative bleeding, postoperative bleeding and hospital stay.

Clinical outcomes comprised: Postoperative complications included screw graft bleeding, endoleak, infections, any neurological complications or the need for revision surgery.

All data were extracted from included articles' text, tables and figures: Data from articles obtained by the principal investigator were reviewed independently by the supervisors to minimize bias.

Table (1): Study Characteristics.

Study	Time Frame	Study Design	n (Open)	n (Endo.)	Follow up (months)
Frank et al. (2013)	2003-2013	P, OS	437	444	12-24
Siracuse et al. (2014)	2003-2014	P, OS	476	1070	36
Nathan et al. (2015)	2012-2015	R, OS	263	263	40
Rubie et al.	2003-2007	P, OS	703	3826	36
Hong et al.	2000-2003	R, OS	582	460	36
Brian et al.	2007-2012	R, OS	99	235	60
Fabio et al.	2000-2013	P, RCT	286	91	58
Samuel et al.	2008-2013	P, RCT	119	219	10-20
Birch et al.	2000-2006	P, OS	31	31	11-24
Brewster et al.	2002-2005	R, OS	28	28	24
May et al.	2000-2005	R, OS	135	148	60
Treharne et al.	2003-2011	P, OS	104	49	NR
Moore et al	2005-2014	R, OS	100	100	52
Scharrer-Palmer et al.	2006-2009	P, OS	29	31	14
Cohnert et al.	2008-2015	R, OS	37	37	17-22
Becquemin et al.	2002-2006	P, OS	107	73	18
Zarins et al.	2006-2010	P, OS	60	190	12
Nicolas et al.	2000-2007	R, OS	25	25	70
Garcia et al.	2005-2012	R, OS	30	35	24-43
Ho et al.	2006-2008	P, OS	3059	4167	18

RESULTS

I. Literature Search: The literature search from the specified electronic databases identified 179 articles. After application of the inclusion and exclusion criteria, 20 comparative studies were finally included in this systematic review. There were 2 randomized trials and 18 observational studies. Of the 20 studies 12 were prospective and 8 were retrospective. Various other approaches were used in combination with open/ endovascular according to the underlying pathology A total of ***11522*** patients underwent ***EVAR*** compared to ***6746*** patients who underwent conventional ***open technique*** for treatment of infra renal abdominal aortic aneurysm. Follow-up for the included studies ranged from ***6*** to ***60*** months (average ***18*** months).

II. **Operative Outcomes:** Operative parameters were reported in all 20 included studies. These include: ***Operative duration:*** Fifteen trials reported the operative time of EVAR and open repair for AAA patients. The mean operative time for EVAR patients ranged from 135 to 263 min. For open repair, the mean operative time ranged from 133 to 312 min. There is no significant difference in operative time between EVAR and open group *(P = 0.07).* ***Intra-operative blood loss:*** Operative blood loss was reported in 11 studies. All of them reported less blood loss in the EVAR group. The mean blood loss for the EVAR group ranged from 96 mL to 641 mL and was 783 mL to 3400 mL in the open repair group. *(P < 0.00001).* ***Hospital stay:*** Hospital stay was reported in 20 studies with an overall result that favoured EVAR. Two clinical trials were randomized controlled studies and the rest were comparative studies. The mean hospital stay required by EVAR patients ranged from 2.0 to 10.0 days and 4.9 to 15.5 days for open repair patients *(P = 0.0001).*

III. Clinical Outcomes: ***Early secondary procedures :*** Seven studies including one randomized controlled trial reported the frequency of secondary procedure required soon after operation (within same hospital admission or 30 days post-operation). More early secondary procedures were required in the EVAR group. The relative risk for EVAR group was 2.03 (95% CI 1.04 to 3.95, P = 0.04). ***Intensive care unit stay:*** Fourteen trials reported postoperative ICU stay of AAA patients. Patients who underwent EVAR required a shorter ICU stay. The mean ICU stay for EVAR group ranged from 0 to 1.5 days, whereas in open repair group the mean ICU stay ranged from 1.1 to 5 days. *P* < 0.0001) ***Complications: Cardiac morbidity:*** Cardiac morbidity was recorded in 16 studies. Systemic review showed a higher risk of cardiac morbidity after operation in the open repair group. The relative risk of cardiac morbidity for EVAR patients was 0.50 (95% CI 0.39 to 0.62, *P* < 0.00001). ***Respiratory morbidity:*** Risk of

respiratory morbidity was also noted to be higher among the open repair patients as reported by 11 clinical trials. The relative risk of the respiratory complications after operation in EVAR group was 0.20 (95% CI 0.14 to 0.28, $P < 0.00001$).

Renal morbidity: Twelve studies reported renal complications related to operation. There was no significant difference in the risk of renal complication after procedure between EVAR and open repair groups. The relative risk of EVAR patients for post-operation renal complications was 0.71 (95% CI 0.48 to 1.05, $P = 0.09$).

Lower limb ischaemia: The risk of lower limb ischaemia was similar between the two groups according to the data obtained from six studies. The relative risk of lower limb ischaemia for EVAR patients was 2.32 (95% CI 0.39 to 13.81, $P = 0.36$) ***Wound morbidity:*** Nine studies reported wound complications after operation for both groups. There was no significant difference detected between the two groups in terms of wound complication risk. The relative risk of wound complication for EVAR patients was 1.20 (95% CI 0.77 to 1.85, $P = 0.42$) ***Colonic ischaemia:*** Only three studies reported the incidence of colonic ischaemia for both EVAR and open repair patients. The open repair group has a higher risk to develop colonic ischaemia after operation. The relative risk of colonic ischaemia for EVAR patients was 0.4 (95% CI 0.21 to 0.75, $P = 0.004$) ***Graft-related morbidity:*** Graft-related morbidity was also only reported in three studies. EVAR patients has a higher risk of having graft related morbidity with a relative risk 1.78 (95% CI 1.28 to 2.47, $P = 0.0006$).

DISCUSSION

The number of AAA patients that received endovascular repair with stent-graft device increased exponentially after the first successful repair in 1991. Despite the wide application of this treatment method, the first randomized control study comparing EVAR to conventional open repair method was only first published in 2004 by the EVAR trial participants. Subsequently, the Dutch DREAM trial group also published two more randomized control studies in October 2004. Comparative studies of the clinical outcomes of EVAR and open aneurysm repair largely out-numbered the randomized control studies. Thus, we faced a dilemma of selecting only the randomized control studies or including also the comparative studies in this systematic review. If only the randomized control trials were included, we would lose a large amount of clinical information of those comparative studies but the bias that existed in the included studies would be minimized. When both randomized control trials and comparative studies were included, we would have a conclusion generated from most of the studies all over the world, yet more bias of patient selection might interfere with the final result. As there are a huge number of comparative studies contributing a lot of clinical data on this particular issue, we finally decided to include both the randomized control trials as well as comparative studies. One feature of the attractiveness of EVAR treatment for AAA is the less traumatic nature of the procedure. The present systematic review confirmed this belief. EVAR patients had a significantly lower 30-day mortality, shorter hospital and ICU stay, less blood loss or blood transfusion requirement, fewer postoperative cardiac and respiratory morbidities, less colonic ischaemia, and fewer overall postoperative problems compared to open repaired aneurysm patients. The operative time, risk of renal complications and risk of lower limb ischaemia were comparable between EVAR and open repair.

EVAR only had a drawback of higher early secondary procedure rate and higher incidence of graft-related morbidity. EVAR is a more favourable treatment of choice when one looks at the short-term outcomes only. However, there is no significant difference in 1-year and even longer term mortality between EVAR and open repaired patients. A quality of life study by the DREAM trial group showed that there was also no significant difference in quality of life demonstrated between patients who received the two treatment modalities 6 months after the initial operation. Among the 20 comparative and randomized control studies included in this systematic review, most of them reported the short-term clinical outcomes in detail. The mid- and long-term outcomes were reported only in 15 studies. Furthermore, the comprehensiveness of reporting mid- and long-term outcomes was not satisfactory. According to the reporting standard of endovascular aneurysm repair study recommended by the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of the Society for Vascular Surgery/American Association for Vascular Surgery, the survival, rupture free-survival, aneurysm rupture, aneurysm-related death, freedom from aneurysm expansion, freedom from type I and III leaks, prevalence of type II endoleak, prevalence of secondary leak, endograft patency, and technical and

clinical success rate should be reported. Yet only the Zarins group had covered all these outcomes in their study. Moreover, the way to present the mid- and long-term outcome varied among different trials making comparisons for mid- and long-term results difficult. For example, some reported intervention-free survival only and some reported number of secondary procedures required. Even more complicated, some clinical parameters (e.g. percentage of endoleak, frequency of secondary intervention) will change with time and individual studies would use different time frames for reporting. The aim of surgical treatment of un-ruptured AAA is to prevent future rupture and prolong the survival of patients, thus only the mid- and long-term results can prove whether one treatment modality is really effective to treat aneurysm patients.

More prospective studies comparing EVAR and open repair for AAA patients with a long follow-up duration and comprehensive reports of mid- and long-term outcomes is needed to give us more concrete evidence whether EVAR is an effective treatment or not in the long run. Another difficulty to compare open and EVAR treatment is that EVAR is an evolving procedure and the design and quality control of stent-graft device is constantly changing. This systematic review included studies performed at different times of the development of the endovascular technique. The majority of the studies reported results of multiple devices which included early and more modern designs. Some of the reported devices were being withdrawn from the market because of frequent complications.

On the other hand, patient selection for the two treatment groups was not comparable in some of the early studies, more ill and elderly patients were assigned to the EVAR arm. We might need to perform systematic analysis for studies involving the new generation devices only or on a single device so as to provide more evidence for better clinical decisions in AAA patient management in the future.

CONCLUSION

Endovascular repair offers significant benefits to aneurysm patients in the early post-operation period. However, it does not show an advantage over open repair in mid- and long-term outcome. Furthermore, EVAR carries more morbidity and higher cost in the longterm. More randomized control studies focused on long-term outcome of EVAR and open repair aneurysm patients as well as on studies on newer generation devices is needed to provide more information for clinical decisions.

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