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Meta-analysis of Outcomes Following Aneurysm Repair in Patients with Synchronous Intra-abdominal Malignancy

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WHAT THIS PAPER ADDS

The aim of this study was to determine outcomes in patients undergoing abdominal aortic aneurysm (AAA) repair (EVAR or open) who have a synchronous malignancy. Synchronous intra-abdominal cancer is relatively common in patients undergoing AAA repair and surgeons are faced with the dilemmas of what type of repair to offer and in what sequence. The findings support that EVAR is superior regarding short-term mortality. Both EVAR and OAR were associated with significant short-term morbidity, which merits careful planning and close follow-up in this patient group. Future studies should look into the optimal timing of AAA repair, for which few data exist.

Objectives: The management of concomitant intra-abdominal malignancy (IAM) and abdominal aortic aneurysm (AAA) remains a challenge, even though malignancy is common in an elderly population. By means of systematic review and meta-analysis, the aim was to investigate outcomes in patients undergoing open (OAR) or endovascular AAA repair (EVAR) that have a concomitant malignancy.

Methods: A systematic literature review was performed (Medline and EMBASE databases) to identify all series reporting outcomes of AAA repair (OAR or EVAR) in patients with concomitant IAM. Meta-analysis was applied to assess mortality and major morbidity at 30 days and long term.

Results: The literature review identified 36 series (543 patients) and the majority (18 series) reported on patients with colorectal malignancy and AAA. Mean weighted mortality for OAR at 30 days was 11% (95% CI: 6.6% to 17.9%); none of the EVAR patients died peri-operatively. The weighted 30-day major complication rate for EVAR was 20.4% (10.0–37.4%) and for OAR it was 15.4% (7.0–30.8%). Most patients had their AAA and malignancy treated non-simultaneously (56.6%, 95% CI, 42.1–70.1%). In the EVAR cohort, three patients (4.6%) died at last follow-up (range 24–64 months). In the OAR cohort 23 (10.6%) had died at last follow up (range from 4 to 73 months).

Conclusion: In this meta-analysis, OAR was associated with significant peri-operative mortality in patients with an IAM. EVAR should be the first-line modality of AAA repair. The majority of patients were not treated simultaneously for the two pathologies, but further investigation is necessary to define the optimal timing for each procedure and malignancy.

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INTRODUCTION

The management of concomitant abdominal aortic aneurysms (AAAs) and intra-abdominal malignancy (IAM) is challenging. The introduction of endovascular AAA repair (EVAR), which has favourable early and medium-term outcomes,[1,2] has further complicated decision-making in this context. Certain patients may not require surgical resection, but in those that do, the dilemma is whether to treat the AAA first, which risks delaying the treatment of the cancer, or to treat the cancer first with the potential risk of AAA rupture and death. A third option is to treat both pathologies simultaneously, especially if the patient is fit enough to undergo a prolonged procedure. However, simultaneous AAA and cancer procedures may be associated with increased risk of graft infection, especially within the context of synchronous gastrointestinal surgery and open aneurysm repair (OAR). Furthermore, cancer resection is fraught with an increased risk of bleeding as anticoagulation is necessary for aneurysm surgery (OAR or EVAR). This increased risk of bleeding may be offset by an increased hypercoagulable state often associated with malignancy[3]; however, this may compromise the subsequent post-operative graft patency and peripheral thrombo-embolic

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complications following OAR or EVAR. Thus the clinical problem is complex.

Randomised trials have shown short-term superiority of EVAR over OAR[1,2,4] and the majority of patients have anatomy suitable for EVAR.[5,6] In the current minimally invasive era there is a need to determine the effect of malignancy on outcomes following EVAR and the risks of EVAR in patients with concomitant IAM.

Following the above, the aim of this study is to assess mortality and morbidity in patients with a synchronous AAA and an IAM through a systematic literature review and meta-analysis.

METHODS

Search strategy

The Medline (1950 to present), EMBASE (1980 to present), Cochrane Library, and Google Scholar (Timeframe = "Anytime") databases were interrogated (date of electronic search, July 15, 2015) to identify all relevant manuscripts reporting outcomes after AAA repair in patients with a concomitant malignancy. The search was limited to studies in human. Various combinations of MeSH terms, phrases, and free text were used to ensure all relevant articles were identified. The search terms were Cancer, neoplasia, tumo(u)r, abdominal aortic aneurysm. Search terms were combined with the use of Boolean operators (AND, OR, NOT). Titles and Abstracts of all publications identified through the search strategy were screened by A.S., O.A., and R.K. independently and consensus regarding inclusion of each manuscript in the analysis was reached following discussion with the senior authors (A.S., R.D.S., M.J.B.). At this stage, once all relevant publications identified through the online search had been obtained, the references of all manuscripts were also manually searched (by A.S. and R.K.) to identify potential publications that had been missed. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance was adhered to at all stages.[7,8] Authors were contacted twice to obtain missing data; manuscripts not reporting at least peri-operative mortality were not included.

Inclusion criteria

Any papers that reported (and where data could be extracted) patient outcomes on intra-abdominal visceral cancer in the context of AAA were included.

Exclusion criteria

Articles that contained only a single case (i.e., case report) and conference proceedings were excluded. The authors of papers with missing information were contacted to obtain relevant missing data and if no operative outcomes could be obtained, these publications were excluded.

Study selection. Two independent reviewers (R.K., O.A.) selected the appropriate studies for both inclusion and exclusion criteria. Discrepancy between reviewers was resolved by a third independent author (A.S.). No specific quality criteria were applied when excluding articles, given that no prospective randomised articles were identified and all relevant publications consisted of case series, mostly of retrospective nature. The Newcastle–Ottawa scale[9] was used to assess study quality by examining patient selection methods, comparability of groups, and assessment of outcome. None of the series included in the eventual analysis achieved a rating of more than four stars.

Definitions

AAA was defined as aortic diameter exceeding 3.0 cm on cross-sectional imaging. Complications and other patient and procedural characteristics were defined using the reporting criteria by Ahn et al.[10] and Chaikof et al.[11] for OAR and EVAR.

Outcome definitions

The primary outcome measure was 30-day mortality. Further outcomes extracted from the articles included aneurysm-related complications (graft limb occlusions, reinterventions, endoleaks, and sac expansions) during the peri-operative period and long-term follow-up, overall patient survival, and major complications; all events are reported using the aforementioned reporting criteria.[10,11]

Statistical analysis

Analyses were performed using the R Package for Windows (version 3.0). Continuous variables of interest are reported using mean values and standard deviation (SD) or median values and range, for parametric and non-parametric data, respectively. Random or fixed effects meta-analysis was performed using the proportions of patients who experience an event (inpatient or 30-day mortality) as outcome data, as necessary, based on between-study heterogeneity. The latter was assessed using the I^2 statistic, which describes the percentage of total variation across studies that arises because of heterogeneity rather than chance or random error. A value greater than 50% was considered to reflect significant heterogeneity owing to real differences in study populations, protocols, interventions, and outcomes for the purposes of this study and hence a random effects model was used in this case. A p value $< .05$ was considered statistically significant. The Newcastle–Ottawa scale[9] was used to assess study quality.

RESULTS

Search results

The initial electronic search identified a total of 658 potential journal articles and after removal of 27 duplicates, a total of 631 unique article titles and abstracts were reviewed, as described above. From this, 258 were deemed to be suitable for full text review. Following that, we identified 36 case series (analysed in 29 separate publications) meeting our inclusion and exclusion criteria (Fig. 1).[12–41] Regarding exclusion of non-intra-abdominal

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