The influence of aneurysm size on early outcome of abdominal aortic aneurysm repair in female patients

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AIM: *The purpose of this study was to examine the influence of aneurysm size on early outcome in women undergoing abdominal aortic aneurysm (AAA) repair, with suggestion of lowered threshold for intervention.*
PATIENTS AND METHODS: *Retrospective cohort study on the early outcome of 25 females undergoing elective endovascular (EVAR) and open AAA repair, compared to 340 males from 2005 to 2017. The study was focused on 30-days mortality (primary endpoint) and incidence of non fatal major adverse events – MAE (secondary endpoint) of two subgroups of women: AAA diameter <50 mm (n.14, group F1), AAA diameter ≥ 50mm (n.11, group F2).*
RESULTS: *The incidence of the primary endpoint at 30 days was 4% in females, and 1.1% in males, respectively (p=ns). Similarly, females showed a higher rate of MAE compared to males (16% vs 9.4%, p=ns). Women who underwent surgery with small aneurysms (F1 group) had an early outcome similar to men (30-day death 0% vs 1.1%, p=ns; MAE 7.1% vs 9.4%, p=ns) and significantly better than women with larger aneurysms (30-day death 0% vs 9%, p=ns; MAE 7.1% vs 27.2, p=ns).*
CONCLUSIONS: *Although poorly significant from a statistical point of view, the present report seems to confirm that the AAA diameter is a relevant marker of disease severity in women, assuming that repair at smaller size may be associated with less comorbidity and better outcome.*

KEY WORDS: Abdominal aortic aneurysm, Abdominal aortic aneurys open repair, Endovascular aortic aneurysm repair, Female gender

Sex differences have been reported in clinical presentation and outcome of women with abdominal aortic aneurysm (AAA). Many studies have shown a worse outcome following endovascular (EVAR) or open (OR) repair of non ruptured AAA for female gender compared to males, suggesting the need to improve the manegement of AAA repair in women (1-4). Although the native aorta is smaller in female gender (16-18 mm vs 18-20 mm), AAA repair in women is actually performed for an aneurysm size quite similar to men (50-55 mm). As a consequence, women undergo AAA repair with a more advanced stage of disease, considering that the aneurysm size is regarded as significative marker of atherosclerotic disease and strictly related to outcome (3, 5, 6). The purpose of this study was to examine the influence of aneurysm size on early outcome in women undergoing AAA repair, with suggestion of lowered threshold for intervention.

Patients and Methods

STUDY DESIGN

This is a retrospective cohort study on the early outcome of 25 females undergoing elective EVAR and open AAA repair from 2005 to 2017. Basing on AAA size,

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determined on transverse axis as maximal outer-to-outer diameter, the study was focused on 30-days outcome of two subgroups of patients: AAA diameter <50 mm (n.14, group F1), AAA diameter ≥ 50mm (n.11, group F2). Three hundred forty males undergoing elective EVAR and open AAA repair in the same period of time was identified as control group by querying our institutional database. Patients were excluded from data retrieval if having urgent/emergent surgery or proximal extension of aortic disease (juxtarenal, pararenal, suprarenal, and type IV thoracoabdominal aneurysm).

Operative Details

OR was performed in usual fashion (endoaneurismectomy + straight/bifurcated prosthetic graft implantation), using general anesthesia and transperitoneal approach. EVAR was performed using standard bifurcated endografts, employing a bilateral femoral cut-down and local anesthesia. Single antiplatelet therapy was maintained in all patients, as usual.
Patients undergoing OR were sent to the postoperative ICU for a closer monitoring of cardiovascular system in the next 24 hours. Patients undergoing EVAR were sent to the ward. According to our postoperative protocol, ECG and blood samples were obtained to evaluate chemical signs of myocardial distress immediately after AAA repair and 24/48 hours later, as well as in patients referring any retrosternal chest pain.

Outcome

Postoperative myocardial infarction: elevation of biomarkers (troponin) associated with clinical symptoms, ECG changes, or regional contractility anomalies.
Major bleeding: haematoma requiring abdominal or inguinal surgical revision.
Pulmonary complications: prolonged ventilation (>48h) or pneumonia requiring prolonged antibiotic therapy (>72h).
Gastrointestinal complications: gastrointestinal bleeding or bowel ischemia.
Renal failure: elevation of creatinine (>2.5 mg/dl) associated with or without oligoanuria.
Critical limb ischemia: peripheral ischemia requiring surgical or endovascular revascularization.

Endpoints

The primary endpoint was the 30-day mortality. Secondary endpoint was incidence of non fatal major adverse events (MAE), including myocardial infarction, major bleedings, pulmonary complications, gastrointestinal complications, renal failure and critical limb ischemia.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as numbers with percentage. Associations between categorical variables and perioperative outcomes in the two groups were tested by using Chi square test with Yates correction and Fisher exact test. A p-value <0.05 was considered statistically significant.

Results

The baseline demographic characteristics showed that females were older (73.3 ± 9.9 *vs* 71.2 ± 7.1 years) and more sick in terms of renal function compared to males (*p=ns,* Table I). The subgroup of women with small aneurysms (<50 mm subgroup F1) resulted younger (69.7 ± 11 years) and with no significative comorbidity difference compared to men, except for renal impairment (*p=ns*). Women with aneurysm size ≥ 50 mm resulted older and presented with a worse clinical status, mainly in terms of renal function (*p<0.05,* Table II).

Table I - *CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.*

	Study Group F n.25	Control Group M n.340
AAA diameter (mean)	52 mm (35-65)	55 mm (25-65)
Age (years)	73.3 ± 9.9	71.2 ± 7.1
CAD (%)	11 (44)	162 (47.6)
Diabetes (%)	2 (8)	37 (10.8)
COPD (%)	12 (48)	139 (40.8)
Hypertension (%)	20 (90)	320 (94.1)
Dyslipidemia (%)	18 (72)	251 (73.8)
CRF (%)	9 (36)	63 (18.5)

Table II - *CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.*

	Group F1 n. 14	Group F2 n. 11	Control Group M n. 340
AAA diameter	42 mm (35-49)	58 mm (50-65)	55 mm (25-65)
Age (years)	69.7 ± 11	78 ± 5.6	71.2 ± 7.1
CAD (%)	6 (42.8)	6 (54.5)	162 (47.6)
Diabetes (%)	1 (7.1)	1 (9)	37 (10.8)
COPD (%)	6 (42.8)	6 (54.5)	139 (40.8)
Hypertension (%)	11 (78.3)	9 (81.8)	320 (94.1)
Dyslipidemia (%)	11 (78.3)	7 (63.6)	251 (73.8)
CRF (%)	4 (28.5)	5 (45.4)*	63 (18.5)*

*p 0.0419

TABLE III - *EVAR, endovascular aneurysm repair; OR, open repair; MAE, major adverse events.*

	Study Group F n. 25	Control Group M n. 340
EVAR (%)	11 (44)	194 (57)
OR (%)	14 (56)	146 (43)
Death (%)	1* (4)	4^ (1.1)
MAE (%)	4 (16)	32 (9.4)

* 1 OR; ^ 3 EVAR, 1 OR; All p = ns

TABLE IV - *EVAR, endovascular aneurysm repair; OR, open repair; MAE, major adverse events.*

	Group F1 (<50mm) n. 14	Group F2 (≥50mm) n. 11	Control Group M n. 340
EVAR (%)	7 (50)	4 (36)	194 (57)
OR (%)	7 (50)	7 (64)	146 (43)
Death (%)	0	1 * (9)	4^ (1.1)
MAE (%)	1 (7.1)	3 (27.2)	32 (9.4)

* 1 OR; ^ 3 EVAR, 1 OR; All p = ns

EVAR was performed in 11 of 25 females (44%) and 194 of 340 males (57%), with technical success in 100% of cases. The incidence of the primary endpoint at 30 days was 4% in females, and 1.1% in males, respectively (*p=ns*). Similarly, females showed a higher rate of MAE compared to males (16% *vs* 9.4%, *p=ns*, Table III). Considering the female subgroups, the early outcome of women who underwent surgery with small aneurysms (F1 group) resulted quite similar to men and significantly better than women with larger aneurysms (F2 group), although the suitability of EVAR remained lower than males (Table IV).

Discussion

Since 1995 many studies have shown a worse early outcome following EVAR or OR of non ruptured AAA for female gender compared to males [1-4,6,7], whereas gender is not a significative risk factor for long-term survival [8]. A recent systematic review focused on outcomes only in studies published since 2009 (1) shows that the 30-day mortality in women is double than of men for both EVAR (2.3% vs 1.4%) and OR (5.4% vs 2.8%). A more advanced age at the time of AAA repair, high comorbidity, type of clinical presentation, and type of repair are main reasons for gender-specific differences in the outcome of AAA surgery.

Some Authors have suggested that aneurysm of certain diameter in women represents more advanced disease than the same-sized aneurysm in man, advising a smaller threshold for AAA intervention to treat earlier female patients who might have a better outcome [1,9,10]. The results of our study seems to confirm this opinion. Against substantial gender differences in terms of comorbidity, 30-day mortality, and occurrence of MAE (Tab. I, II, III), females who underwent surgery with AAA <50 mm, showed less comorbidity and better outcome compared to those undergoing larger aneurysms repair and the 30-days mortality and MAE resulted similar to male group (Table II, IV). Contrariwise, according to other reports [11,12], we observed that hostile anatomy (short neck length, neck angulation and small iliac access) is still present in women independently from the aneurysm diameter, as EVAR resulted still not feasible in a substantial number of patients even after adjustment for aneurysm size (50%, Table IV). The low elegibility to EVAR may be regarded as a key point to explain the worse outcome in female gender undergoing AAA repair. However, new endovascular technologies would be able to treat more hostile anatomy in females with consistent effects on surgical indication and outcome. The ENGAGE registry, evaluating Endurant endoprosthesis (Medtronic, Inc. 710 Medtronic Parkway Minneapolis, MN 55432 USA) on 157 females with AAA (mean diameter 57.9±9.6) reported similar early and 5-years outcomes compared to males, with notable minimal differences in terms of type I endoleaks (3.8% vs 1.3%) and equivalent long-term survival [13,14]. Likewise, the LUCY study, focused on 76 females (mean AAA diameter 50.2±6) undergoing EVAR with Ovation endoprosthesis (Endologix, Inc. 2 Musick, Irvine CA 92618 USA), reported no significative gender differences compared to 149 males, in terms of early/late type I endoleak (respectively 2% in women vs 0% in men, 1.4% in women vs 2.1 in men) and showed no aneurysm-related mortality through follow-up [15,16].

The debate to determine whether up-dated treatment indications should be considered for female AAA repair is ongoing, as we need to improve the outcome in women. The decision to lower the threshold for aneurysm repair in females seems actually much more suitable for addressing the gender associated risk, but must be weighed against the lack of any randomized data and evidence of no well-defined indication from UK-SAT, OVER, ADAM, and DREAM trial where the group of women was numerically small [18-21]. Further study on the natural history and ideal threshold for repair of female AAA are advocated to achieve gender-specific guidelines.

Conclusions

The outcome after surgery for AAA is less favorable in women with significantly reduced long-term survival and a trend to increased 30-day mortality.

A more advanced age at the time of AAA repair, high

comorbidity, type of clinical presentation, and type of repair are main reasons for gender-specific differences in the outcome of AAA surgery.
As the comorbidity and outcome of aneurysm repair is strictly related to the aneurysm size, the decision to lower the threshold for aneurysm repair in females seems actually much more suitable to improve the surgical results in women.
Further study on the natural history and ideal threshold for repair of female AAA are advocated to achieve gender-specific guidelines.

Study limitations

This study is retrospective and this is the main limitation. Moreover, the small number of females undergoing AAA repair affected the statistic value and the observations should be tested on a large population study.

Riassunto

Introduzione e Scopo dello Studio: Il sesso femminile, influenza in senso sfavorevole la presentazione clinica ed i risultati del trattamento per aneurisma dell'aorta addominale (AAA). In particolare, le donne candidate al trattamento chirurgico di AAA risultano affette da comorbidità significativamente maggiore rispetto agli uomini e, indipendentemente dal tipo di tecnica utilizzata – chirurgica tradizionale od endovascolare, manifestano un tasso doppio di complicanze e mortalità rispetto al sesso maschile. Poiché il diametro dell'AAA è direttamente correlato all'incidenza di comorbidità ed alla prognosi, un'indicazione chirurgica più precoce per il sesso femminile, potrebbe associarsi ad un migliore risultato del trattamento. Lo scopo di questo studio è stato quello di valutare l'influenza del diametro dell'AAA su mortalità ed incidenza di complicanze a 30 giorni dalla correzione chirurgica od endovascolare nel sesso femminile.
Materiali e Metodi. Studio retrospettivo su 25 pazienti di sesso femminile sottoposte a chirurgia in elezione per AAA (2005-2017), con tecnica tradizionale (OR) od endovascolare (EVAR). Sono stati individuati due sottogruppi di donne: 14 pazienti con diametro dell'AAA inferiore a 50 mm (group F1); 11 pazienti con diametro dell'AAA uguale o superiore a 50mm (group F2). Come gruppo di controllo, sono stati individuati 340 maschi sottoposti in elezione nello stesso arco di tempo ad EVAR od OR. Endpoint primario: mortalità a 30 giorni nel gruppo femminile e nei sottogruppi F1 e F2. Endpoint secondario: incidenza a 30 giorni di eventi non fatali (MAE) nel gruppo femminile e nei sottogruppi F1 e F2.
Risultati: Globalmente il gruppo di sesso femminile risultava di età più avanzata (73.3 ± 9.9 *vs* 71.2 ± 7.1) e maggiormente affetto da comorbidità significativa rispetto al sesso maschile, soprattutto in termini di ridotta funzione renale (36% *vs* 18%, *p=ns*) e presenza di bronchite cronica ostruttiva (48% *vs* 40.8%, *p=ns*). L'incidenza degli endpoint primario e secondario risultava più elevata per il sesso femminile rispetto al sesso maschile (endpoint primario 4% *vs* 1.1%, *p=ns;* endpoint secondario 16% *vs* 9.4%, *p=ns*). Il sottogruppo di femmine sottoposte alla correzione di AAA < 50 mm (gruppo F1) manifestavano una prognosi molto simile a quella dei maschi (endpoint primario 0% *vs* 1.1%, *p=ns* ; endpoint secondario 7.1% *vs* 9.4%, *p=ns*) e migliore rispetto alle pazienti sottoposte ad intervento con AAA ≥ 50 mm (endpoint primario 0% *vs* 9%, *p=ns* ;endpoint secondario 7.1% *vs* 27.2%, *p=ns*).
Discussione e Conclusioni. La prognosi dopo chirurgia per AAA risulta generalmente meno favorevole per il sesso femminile. Anche senza una solida significatività statistica, i risultati del presente studio sembrano confermare che nel sesso femminile il diametro dell'AAA è direttamente correlato alla comorbidità ed alla prognosi, in quanto le pazienti sottoposte alla correzione chirurgica od endovascolare con diametro < 50 mm manifestano una prognosi del tutto simile a quella dei maschi. In accordo con altri dati di letteratura, il nostro studio suggerisce l'opportunità di studi prospettici, adatti a riconsiderare il diametro minimo per l'indicazione chirurgica dell'AAA per il sesso femminile, con lo scopo di condizionare favorevolmente i risultati del trattamento.

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