



Title	Long-Term Outcome of Single Institutional Experience with Conservative and Surgical Management for Renal Artery Aneurysm
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(1) title

Long-term outcome of single institutional experience with conservative and surgical management for renal artery aneurysm

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Indication criteria for active surveillance of renal arterial aneurysm

Key words

Renal arterial aneurysm, conservative therapy, intervention, surgical repair, outcomes, criteria

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Abstract

Backgrounds: Spontaneous rupture risk in renal arterial aneurysm (RAA) is extremely low. Indication criteria for surgical repair of RAA remain uncertain. **Objective:** Long-term outcomes of conservative therapy and surgical repair were evaluated. **Patients:** The study included fifty-eight patients (17 male, 41 female) diagnosed with RAA during the last 21 years. Median age at the time of diagnosis was 62 (19-85) years old, and the median follow-up period was 69 (3-216) months. **Methods:** The patients were divided into two groups; conservative group (n=30) who had been followed up with blood pressure control, and treatment group (n=29) who underwent intervention. **Results:** Multiple efferent aneurysmal branches were found in seven conservative cases and 16 treatment cases (p=0.002). The median maximum diameter of aneurysm was lower in conservative group than in the treatment group (15 versus 25 mm, p=0.005). Two cases in conservative group showed increase in aneurysm size during follow-up. Hypertensive state had been essentially no change in both groups during follow-up. Renal function decreased with age similarly both in conservative and treatment groups. **Conclusions;** Our conservative management criteria for RAA are justifiable and even too strict. More loose criteria will be pursued in conservative group selection.

Introduction

The incidence of renal arterial aneurysm (RAA) is estimated at 0.09% in the general population 1). RAA (most often resulting in renal infarction) was found incidentally at autopsy in 7-12% of patients who died of cardiovascular disease 2). Because the risk of spontaneous rupture is extremely low in RAA relative to other arterial aneurysms, indication criteria for surgical repair of RAA remain uncertain. Furthermore, no long-term follow-up studies of active surveillance for RAA have been reported. In order to confirm the reliability and safety of RAA surgical criteria of

our institution, we have assessed the health of patients with incidental RAA for several decades. In this study, we evaluate the long-term incidence of adverse events and outcomes between patients with active surveillance and with surgical treatment.

Patients and Methods

Between 1989 and 2009, fifty-eight patients (17 male and 41 female) at our institute were diagnosed with RAA. Four of the patients had bilateral disease, for a total of 62 RAAs presented. The median age for first visit to our institute was 62 years old (range 19-85), and the median follow-up period was 69 months (range 3-216).

At the first visit, a CT scan was performed on all patients. In addition, 47 patients (81.0%) underwent renal scintigram (99m-Tc-Diethylenetriamine pentaacetic acid; 40, Mercurioacetyl triglycine; 4, Dimercaptosuccinic acid; 3) and 35 patients (60.3%) underwent angiography. Renal scintigram was scheduled routinely in order to evaluate total GFR and split renal function, while 11 patients failed to receive. Angiography was performed in selected patients in order to know precise RAA structural characteristics which was not unclear in regular CT scan. General laboratory tests, including serum creatinine or creatinine clearance, allowed calculation of the glomerular filtration rate (GFR) as well as the 99m-Tc DTPA-GFR. RAAs were evaluated with regard to their location, morphology, number of efferent branches, maximum diameter and degree of calcification. Any patients with simultaneous renal tumor, renal arteriovenous fistula, or pseudoaneurysm of the renal artery were excluded.

Detailed RAA characteristics are presented in Table 1. In 36 cases, the RAA was located in the main trunk of the renal artery. RAA morphology included 29 cases of the saccular type and 33 of the fusiform type. Multiple efferent branches were observed in 23 of 62, and the maximum aneurysmal diameter ranged from 8 to 56 mm (median 18 mm). Fifty of the 62 RAAs showed partial or circumferential calcification of the RAA wall. All patients underwent screening

for extrarenal aneurysm by CT scan and neurosurgery consultation. Among all 58 patients, seven showed co-existing extrarenal arterial aneurysms in the following locations: two in the abdominal aorta, two in the common iliac artery, one in the splenic artery, one in the carotid artery and one in the cerebral artery. Patients' associated diseases included one case of Marfan syndrome, one of neurofibromatosis, one case of syphilis, and one live kidney donor candidate.

Patients were divided into the conservative group (30 patients, 34 RAAs) or the treatment group (29 patients, 29 RAAs). Our institutional guidelines for inclusion in the conservative group consisted of patient age (40 years or older), maximum RAA diameter (under 20 mm), and calcified RAA. Patient had been followed up by annual examination including CT scan, or ultrasonography, and laboratory tests under strict blood pressure control with anti-hypertensive medications. The numbers of treatment-group patients who initially underwent specific surgical RAA repairs are as follows (Table 2): 20 patients with ex-vivo RAA repair with auto-transplantation, four patients with in situ RAA repair, three with nephrectomy. Two patients underwent transluminal embolization.

Patients' backgrounds, including gender, age at diagnosis, symptom, hypertension, alcohol and smoking habit, body mass index and evaluation period, are presented in Table 3. The median age of diagnosis in the conservative group was significantly older than in the treatment group ($p=0.034$). There was a significantly higher history of smoking among patients in the treatment group than in the conservative group ($p=0.024$). The two patient groups showed no other statistically significant differences in backgrounds. Eighteen and twenty-three patients of the two groups had been diagnosed as RAA incidentally. Their onset of incidental finding was made by imaging tests during investigations for gall-bladder stone (9), dry doc (8), gastro-intestinal disease (7), urological work up (6), staging of malignant disease (3), diabetes mellitus (2), and others (6).

We evaluated RAA characteristics, patient survival, adverse events and co-morbidity,

outcome of blood pressure control and renal function for these two groups. The study was approved by the Ethical Review Board of Hokkaido University Hospital and conducted in accordance with the Helsinki Declaration.

Results

RAA characteristics

The conservative group included four cases of bilateral kidney involvement. There were no statistical differences in RAA characteristics (laterality, location, morphology, degree of calcification) between the groups. However, there was higher number of efferent branches in treatment group than that in conservative group ($p=0.002$). Maximum aneurysmal diameter in treatment group was higher than that in conservative group ($p=0.005$) (Table 4).

Patient survival, RAA change, adverse events and co-morbidity

Two patients in the conservative group died due to non-RAA-related causes. A 68 years old male had a 15-mm, saccular, partially calcified RAA in the right renal artery bifurcation. He had presented microscopic hematuria throughout a follow-up period, and died at age 76 from cerebral infarction. A 77 years old female had a 10-mm, saccular, partially calcified RAA in the left renal artery bifurcation, died at age 82 due to non vascular disease. In both patients, RAA size did not change during the observation period (8 and 5 years, respectively).

RAA in 2 of conservative group increased during the evaluation period. During the ten-year follow-up period of a 65 years old female with no hypertension, the size of a 10-mm-diameter, fusiform, non-calcified RAA in her left renal artery trunk increased only to 13 mm. Similarly, during the three-year follow-up period, 12 mm non-calcified fusiform RAA of 53 years old female taking anti-hypertensive medication in her right renal artery bifurcation increased to 15 mm. In addition to these two cases, a 66 years old woman in the conservative group does

not consented to undergo surgical repair of a 31-mm, fusiform, partially-calcified RAA in the renal artery bifurcation of right kidney. She has shown no change of RAA size in the last 3 years. No other adverse event was recorded in all patients of conservative group (Figure 1).

There were no deaths in treatment group. Fifteen of the 27 patients (55.6%) who underwent surgical RAA repair experienced the following post-operative adverse events: auto-transplanted kidney atrophy due to renal arterial stenosis (two cases), partial renal infarction in auto-transplanted kidney (two cases), renal arterial anastomosis site stenosis which needed percutaneous transluminal arterioplasty (four cases), ureter stenosis or vesico-ureteral reflux of auto-transplanted kidney (each 1), wound herniation which needed surgical repair (three cases) and intractable pain of surgical wound (two cases). These adverse events had occurred at later than a month post-operatively, except for 2 cases (partial renal infarction in auto-transplanted kidney and ureter stenosis of auto-transplanted kidney).

Outcome of blood pressure control and renal function

Among patients of both groups, hypertension was under good control during entire evaluation period. In the conservative group, two patients needed an increased dose of anti-hypertensive medication. There were no patients who deteriorated blood pressure control after RAA surgery except just one normotensive patient in the treatment group who began taking anti-hypertensive medication post-operatively. Compared to the initial GFR, the current GFR in both groups significantly decreased ($p=0.008$ and $p=0.0001$, respectively), but there was no significant difference in the degree of GFR change between the two groups (Figure 2).

Discussion

This retrospective study was conducted in an effort to assess the long-term outcomes of conservative therapy and initial surgical treatment of RAAs, and to study the parameters of patient

selection for these groups. Our decision to determine who should undergo surgical or interventional treatment is decided by patient age, the size and calcification degree of RAA. The results of this study showed no adverse events among patients in the conservative group. Based on the results of our study, we will expand the criteria limits for conservative policy rather than surgically (e.g.; surgical treatment should be performed only in patient who has any of following factors with 40 years or younger, pregnant woman, or progression in size of RAA during the annual follow-up in conservative group).

In the performance of comparisons between patient groups, there are clinical limitations in the random and controlled aspects since there were some cohort differences between the two groups in our study (i.e. age at diagnosis, number of efferent branches, and maximum diameter of RAA). In the largest reported study of RAA treatment [involving 168 patients (107 women, 61 men) treated over a 35-year period], 15% of patients showed a history of tobacco use, 6.5% experienced aneurysms in an extrarenal lesion, 73% had hypertension, and 55% were asymptomatic 3). Thirty-two patients (19%) had bilateral RAAs, while 60% of the remaining monolateral RAAs were right-sided and 40% were left-sided. For morphology, 79% of the RAAs were saccular and 21% were fusiform, and the incidence of non-calcification among all RAAs was 62.9%. Only three patients presented with acute overt RAA rupture. They selected 47 patients (28.0%) for the observation group and the remaining patients were treated surgically. Although most patients experienced improved post-operative control of hypertension, precise evaluation of long-term complications was not investigated.

Comparing to this study, our patient group showed a more frequent history of smoking (40.8%), a higher incidence of extrarenal disease (12.0%), less number of hypertension (60.3%) and more asymptomatic cases (69.5%). Only 6.9% of our cases were bilateral, and 55% of monolateral cases were right-sided. Relative to the previous study, RAAs showed a lower incidence of saccular morphology (46.8%) and of non-calcification (19.4%).

Although little is known about the natural history of clinically silent RAA, there have been incidences of RAA rupture reported in cases with renovascular hypertension, distal renal arterial thrombosis and infarction, and arteriovenous fistula 4). Only pregnancy and late-age atherosclerosis have been reported as associated conditions that enhance the risk of RAA rupture 4, 5). Because clinically controlled studies of risk factors are not performed for ethical reasons, we clinicians must decide on interventional treatments based on other indications. There is a difficulty in a prospective study for such an uncommon disease. Recommended indicative factors for aggressive treatment generally include age, gender, symptoms, degree of hypertension, RAA size and its progression, renal function, and anatomical complexity 4, 6). We had established our institutional criteria for active surveillance based on these factors.

The incidence of surgical complications in our study is higher than in earlier reports 3, 7). One possible cause could be that greater surgical damage occurred in elder patients who underwent nephrectomy followed by ex vivo RAA repair and autotransplantation at our institution. Although recent, less invasive endo-vascular techniques have been reported, our current institutional policy favors arterial reconstruction as the primary treatment of anatomically complex RAAs 6, 8). The incidence of wound herniation and post-operative wound pain could be avoided by combination of laparoscopic nephrectomy and auto-transplantation.

Based on our findings from long-term analysis of RAAs in the conservative group, our criteria for conservative management of RAA were safe enough result. We now plan to expand the criteria for selection of patients for active surveillance and strict blood pressure control relative to surgical treatment. Considering current outcome in this study, surgical criteria of; childbearing female, 40 years or younger, or progression in size of RAA during the annual follow-up in conservative group would be reasonable. We will perform surgery for RAA patients under the new criteria and follow up the conservative group cases carefully, and consider interventions in the case whose RAA size is increasing.

Conclusions

This retrospective study describes the long-term outcomes of conservative therapy versus initial surgery for RAAs. Since our indication of surgical or interventional treatment was decided by patient age, size and degree of RAA calcification, we observed a significant difference in patient and RAA characteristics between the conservative and treatment groups. Based on the fact that patients in the conservative group experienced no adverse events, we are considering to expand our criteria for active surveillance.

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Figure legends

Figure 1. GFR changes

Initial GFR of both groups decreased at the current observation time. There was no significant difference in the degree of GFR change between the two groups.

Figure 2. Treatment selection and patient survival

All RAA patients (58 cases) were divided into two groups (conservative group; 30 and treatment group; 28). Only 2 of 30 patients in conservative group has presented RAA size increasing. One case (57 years old woman, conservative group) with 15-mm diameter fusiform RAA in the second bifurcation of right renal artery had been followed up for 17 years and underwent ex-vivo repair. All patients are alive except for only 2 cases who died from non-vascular disease in conservative group.

Figure 1.

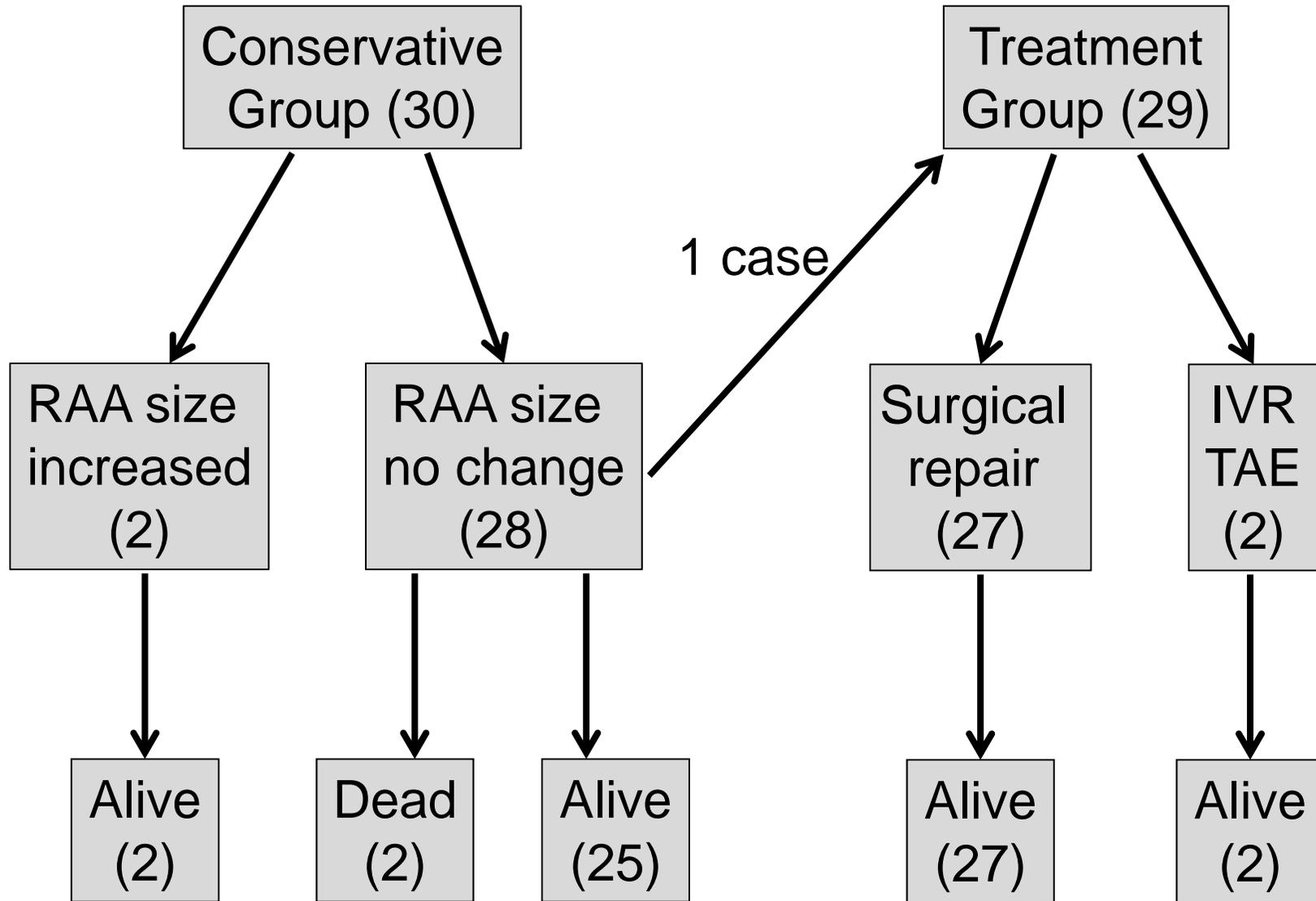


Figure 2.

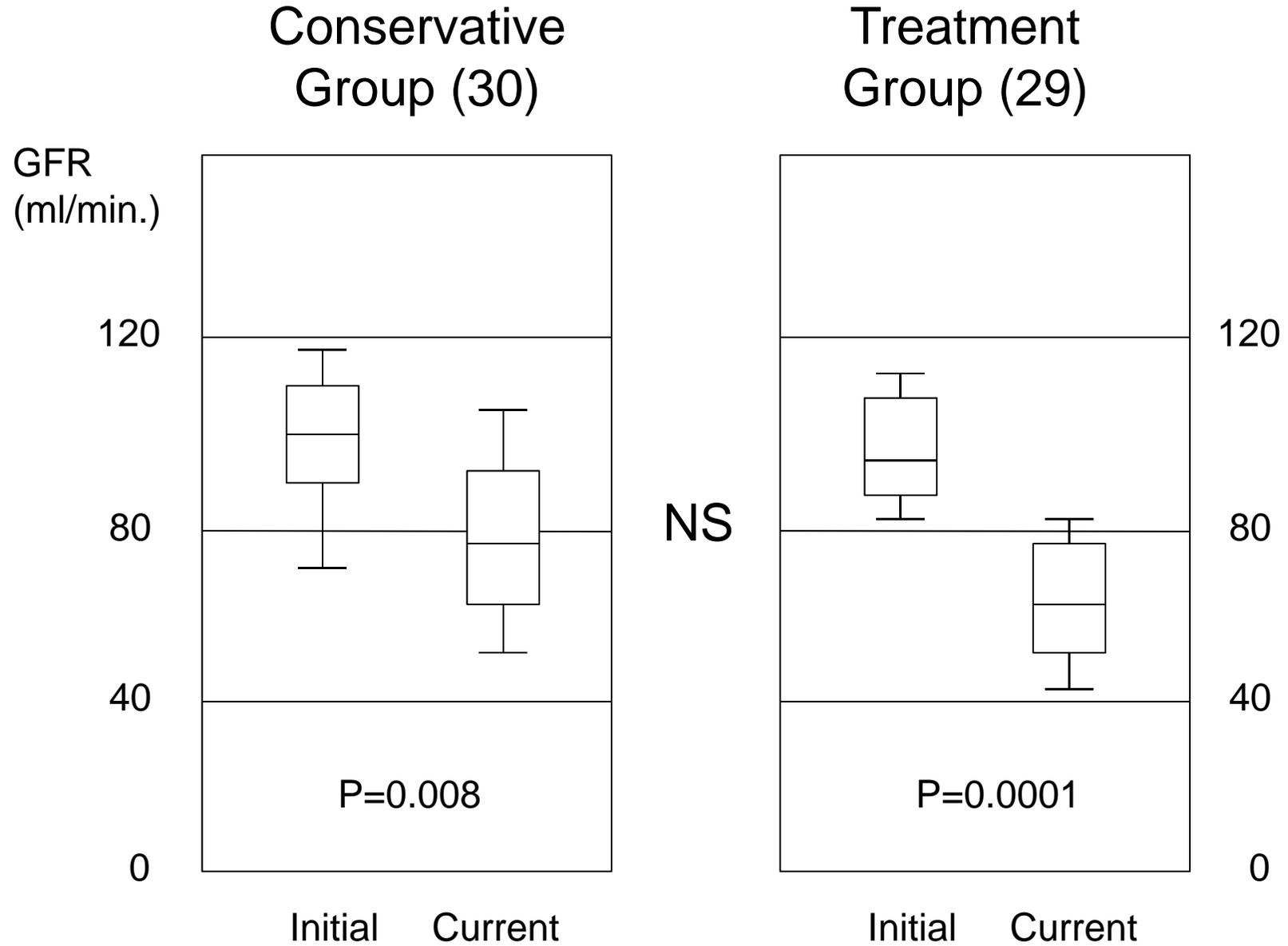


Table 1. Patient background and characteristics of renal artery aneurysm

Sex	Female	41
	Male	17
Laterality	Bilateral	4
	Right	30
	Left	24
Location	Main trunk	36
	First branch	24
	Second branch	2
Morphology	Saccular	29
	Fusiform	33
Number of efferent branches	None	16
	1	20
	2	9
	3	13
	4	1
	Unclear	3
Maximum diameter	18 mm (median),	8-56 mm (range)
Calcification	None	12
	Partial	41
	Circumference	9

Table 2. Treatment group (n=29)

Surgical repair (27)	Ex-vivo repair	20
	In situ repair	4
	Nephrectomy (3)	Renal collapse during laparoscopic nephrectomy *1
		Emergent nephrectomy with massive hematuria *2
Ex-vivo repair and allo-transplantation *3		
Intervention radiology (2)	(IVR)	Transluminal embolization with coil stent *4

*1 We scheduled laparoscopic right nephrectomy and consecutive ex-vivo aneurysmal repair followed by auto-transplantation for 50 years old woman with 33 mm diameter RAA. During the nephrectomy, collateral artery spasm drove renal collapse and resulted in nephrectomy alone because the kidney was not available for auto-transplantation.

*2 Seventy-three years old woman arrived at our institution with massive macrohematuria and pre-shock condition. CT scan revealed left RAA (56 mm diameter) perforated into urinary collecting system. Renal scintigram showed low split renal function (11.7%). She underwent emergent nephrectomy at the next day of her arrival.

*3 Live kidney donor (61 years old woman with 9 mm RAA) underwent nephrectomy. RAA was removed and the kidney graft was transplanted to her son following ex-vivo repair using the recipient's hypogastric artery.

*4 Two patients with representative saccular RAA moved to IVR section. They (77 years old man and 58 years old woman) had incidentally diagnosed saccular RAA with maximum diameter 35 and 28 mm, circumferential calcification, and no efferent branch. They underwent transluminal coil stent embolizations uneventfully.

Table 3. Patients' backgrounds between conservative and treatment group

		Conservative group (30)	Treatment group (29)	
Sex	Female	22	20	N.S.
	Male	8	9	
Age at diagnosis	Median	65	58	p=0.034
	Range	39-85	19-77	
Symptom	Hematuria	4	2	N.S.
	Abdominal pain	5	3	
	Hypertension	3	1	
	Incidental	18	23	
Hypertension	No	12	11	N.S.
	1 drug	12	10	
	2 or more drugs	6	3	
Alcohol habit	No	9	11	N.S.
	Yes	13	15	
Smoking habit	No	18	11	p=0.024
	Yes	5	15	
Body mass index (kg/m ²)	Median	23.7	24.2	N.S.
	Range	16.0-31.4	18.3-29.6	
Follow-up period (months)	Median	65.4	111.4	N.S.
	Range	3-216	3-216	

Table 4. RAA characteristics between conservative and treatment group

		Conservative group (34)	Treatment group (29)	
Laterality	Bilateral	4	0	N.S.
	Right	16	15	
	Left	10	14	
Location	Main trunk	20	16	N.S.
	First branch	13	11	
	Second branch	1	2	
Morphology	Saccular	18	16	N.S.
	Fusiform	16	13	
Number of efferent branches	None	9	7	p=0.002
	Single	16	5	
	Multiple	7	16	
Maximum diameter (mm)	Median	15	25	p=0.005
	Range	8-31	9-56	
Calcification	No	7	5	N.S.
	Partial	19	23	
	Circumference	8	1	