Results of surgical treatment for renovascular hypertension in children: 30-year single-centre experience

Marike B. Stadermann1, Giovanni Moţîni1, George Hamilton3, Derek J. Roebuck2, Clare A. McLaren2, Michael J. Dillon1, Stephen D. Marks1 and Kjell Tullus1

1Department of Paediatric Nephrology and, 2Radiology, Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London, UK and 3Department of Vascular Surgery, Royal Free Hospital, London, UK

Correspondence and offprint requests to: Kjell Tullus; E-mail: tulluk@gosh.nhs.uk

Abstract

Background. We retrospectively reviewed the medical records of all patients who underwent surgery as part of the treatment of renovascular hypertension (RVH) at our centre between 1979 and 2008.

Patients. Thirty-seven children (65% male) with a median age of 7.6 (0.4–17.9) years were identified with a median systolic blood pressure (SBP) of 140 (105–300) mm Hg prior to surgery. Bilateral renal artery stenosis and intra-renal disease were present in 19 (51%) patients, mid-aortic syndrome in 15 (40%), involvement of visceral arteries in eight out of 35 (23%) and coexisting cerebral disease in eight out of 30 (26%) investigated patients.

Results. Surgical procedures (n = 53) included (i) nephrectomy (18, of which two unplanned and two secondary due to technical failure), (ii) renovascular surgery on the renal arteries (28, of which 18 had autologous surgery and 10 synthetic grafts inserted for revascularisation) and (iii) aortic reconstruction with (6) and without (1) a synthetic graft. Post-operative complications were haemorrhage (5), sepsicaemia (5) and chylous ascites (1). There were no perioperative deaths; two children died during follow-up. The SBP post-surgery improved to a median value of 116 (range 90–160) mm Hg. Twelve months after surgery, 16 (43%) children had normal blood pressure without treatment, 15 (41%) normal or improved on one to four antihypertensive drugs and four (11%) unchanged; no data were available for two (5%) children.

Conclusion. Surgery effectively treated the hypertension of 90% of our children, when performed in conjunction with medical therapy and interventional radiology. In spite of aggressive surgical treatment, RVH is sometimes a progressive disease.

Keywords: bypass; children; graft; nephrectomy; renovascular hypertension
Introduction

Renovascular hypertension (RVH) is caused by an arterial lesion(s) that compromises blood flow of one or both kidneys [1–3] and represents 10% of all cases of secondary hypertension in children [4,5]. Renal artery stenosis (RAS) is one of the most common abnormalities observed in children with secondary hypertension [1]. Lesions may not be limited to the main renal arteries but can also involve the intra-renal, coeliac, mesenteric and cerebral vasculature [1,5]. Moreover, there is an association with abdominal intra-renal, coeliac, mesenteric and cerebral vasculature limited to the main renal arteries but can also involve the dren with secondary hypertension [1]. Lesions may not be one of the most common abnormalities observed in children with secondary hypertension [4,5]. Renal artery stenosis (RAS) in 30% of children with RVH [6–9]. Neurofibromatosis type 1 (NF1) [1,7,10] and Williams syndrome [11] predispose to the development of RVH.

The initial treatment of RVH is medical therapy with antihypertensive drugs, although side effects may be encountered with these medications. This happens especially if a normal blood pressure is achieved too rapidly or if drugs acting on the renin-angiotensin axis are utilized reducing the blood flow to the kidney. Medical treatment alone is often insufficient to control hypertension adequately, leaving those children exposed to life-threatening events such as cerebrovascular accidents (CVA) and cardiac failure, and so more aggressive treatments are required. Subsequent interventions may include percutaneous transluminal angioplasty (PTA) with or without stenting. In our centre, an improvement of systolic blood pressure (SBP) was demonstrated in 50% of patients after PTA [12]. Children may benefit from surgical procedures if lesions are too complex for PTA or if PTA fails to achieve long-term control of hypertension [13]. Surgical procedures include nephrectomy, renal artery reimplantation, arterial reconstruction with autologous or synthetic grafts and autotransplantation [5,6,8,13–17].

In order to evaluate the efficacy and the complications of surgery in the treatment of RVH, we evaluated the notes of children treated in our hospital from 1979.

Subjects and methods

In this retrospective study, all children who underwent surgery for RVH were identified from the database at Great Ormond Street Hospital for Children NHS Trust, London. All children underwent an RVH work-up at admission consisting of a detailed medical history, manual blood pressure recording using a mercury sphygmomanometer or the Accuson green light and physical examination with auscultation of head, abdomen and back for bruits, in addition to feeling for pulse deficits and search for clinical features of syndromes. Renal function was assessed with estimated glomerular filtration rate (eGFR) calculated by the Schwartz formula [18]. Proteinuria was defined as a urine albumin/creatinine ratio >10 mg/mmol or a positive dipstick with more than 1+ on more than one occasion.

Abdominal and Doppler renal ultrasound and pre- and post-captopril scintigraphy with technetium-99m dimercaptosuccinic acid scintigraphy (DMSA) were obtained to identify possible renal perfusion defects and relative renal function. Angiography was performed in all patients. Intra-renal disease (IRD) was defined as lesions in intra-renal arteries not amenable to surgery.

Technetium-99m hexamethyl propyleneamine oxime scintigraphy (HMPAO) was used to evaluate cerebral perfusion. Cerebral angiography was performed if clinically indicated. The presence of widespread disease or audible cranial bruits was regarded as a strong indicator to perform angiography for cerebral involvement.

The results of the tests were subsequently discussed with the multidisciplinary team consisting of paediatric nephrologists, interventional radiologists and surgeons. Surgical intervention was only performed in patients when medical and/or endovascular therapeutic interventions had failed or when PTA was not technically possible. The surgical procedure was decided by the patient's surgeon and varied between different time periods. Nephrectomy was performed in children with <10% function in the kidney that was thought to drive up the blood pressure or when no other treatment had been successful in controlling the blood pressure. Long-term aspirin was given to all children after revascularisation procedures.

Outcome measurement

Children living in the UK were followed up with visits to the outpatient clinic at regular intervals with BP measurements. International referrals were followed up by reviews at our hospital.

Outcomes were based upon the criteria by Ellis et al. [19], and children were regarded as (i) “cured” with normal SBP (<95th centile for age, gender and height centile [20]) without medication, (ii) “improved” with lower SBP with the same or reduced treatment and (iii) “unchanged” with the same SBP with the same or increased treatment. The last category (iv) “perioperative failure” was used to describe failure of the attempted surgery or occurrence of graft stenosis or other complications postoperatively leading to a dysfunctional bypass.

We describe both short- and long-term outcomes (surgery outcomes and complications; SBP and medication 1 year after surgery or earlier when children underwent further surgery within 1 year and at the patient’s last visit to the outpatient clinic). The local ethics committee approved the study.

Results

Patients

Thirty-seven children (24 boys) underwent surgery for RVH at a median age of 7.6 (0.4 to 17.9) years and median weight of 24.5 (6.1–64) kg. Patients were tertiary referrals from general hospitals (n = 24, 65%) or quaternary referrals from paediatric nephrology centres from within (n = 3, 8%) or outside (n = 9, 24%) the UK. One patient was referred from the cardiology department of our hospital. The median interval between diagnosis of hypertension and referral to our service was 0.2 (0.0–2.9) years and between referral and surgery 0.6 (0.0 to 4.5) years.

Ten children were asymptomatic at presentation. One of them had suffered from a stroke in the past. Twenty-eight patients presented with one or more symptoms, with headaches (n = 10) and signs of cardiac illness, such as asymptomatic heart murmur or congestive heart failure (n = 8) being the most common features. Underlying syndromes were present in eight children; NF1 in six, Williams syndrome in one and possible Klippel Trenaunay Weber syndrome in one patient. Two children had renovascular lesions secondary to abdominal malignancies.

SBP had normalized with medical treatment in two children before surgery (they had surgery because of unacceptable side effects from the medical treatment) between the 90th and 95th centiles for eight children and above the 99th centile in the remaining 27 children. Median SBP was 140 (105–300) mm Hg for all children who were treated with a median of four (range 2–7) antihypertensive agents. Normal BP could not be achieved or could be achieved only with unacceptable adverse effects. The median eGFR was 93 (range 30–145) ml/min/1.73 m² (Table 1).
Evidence of end-organ damage was present in the majority (75%) of patients, predominantly left ventricular hypertrophy, which occurred in 23 out of 32 patients. Angiography demonstrated bilateral RAS and IRD in 19 (51%) children and MAS in 15 (40%). Involvement of visceral arteries was observed in eight out of 34 (24%) tested patients and coexisting cerebral disease in eight out of 30 (26%).

Surgical history

Six children had undergone a total of six angioplasties and four surgical procedures in other hospitals prior to admission. These children had undergone surgery and/or PTA for abdominal malignancies with compression of the aorta (n = 2), MAS (n = 2), a non-functioning kidney in a child with NF1 (n = 1) and supravalvular aortic stenosis in a child with Williams syndrome (n = 1).

Surgery

A wide variety of surgical procedures were performed in our cohort of patients, as surgical approaches and surgical teams differed considerably during the years (Table 2). For descriptive purposes we distinguish three time intervals: I. 1979–1988, II. 1989–2000 and III. 2001–2008. Fifty-three surgical procedures were performed in 37 patients (Table 2). Seven and two children had two and three operations, respectively. Five children had bilateral procedures simultaneously. In two patients, failed revascularisation procedures led to an unplanned nephrectomy. Reasons for further surgery were the development of new stenotic lesions (n = 8) and technical failures (n = 2).

Renal surgical procedures included primary nephrectomy (n = 13) or hemi-nephrectomy (n = 1), unplanned nephrectomy (n = 2) and secondary nephrectomy (n = 2). Autologous renal revascularisation surgery (n = 18) including autotransplantation in three children, renal artery reimplantation in three, aortorenal bypass surgery with an autologous vein in five and splenorenal, iliac-renal or gastroduodenal-renal bypass in seven children. Reconstruction of the renal artery was performed with a synthetic graft in six children with unilateral RAS. In four children with bilateral RAS, a trouser graft was inserted.

Surgical aortic reconstruction was accomplished with a resection of the stenotic segment and repair of the aorta (n = 1) or with insertion of Gortex patches or interposition grafts (n = 6).

Intra-operative complications

Two procedures encountered complications leading to an unplanned nephrectomy. In one patient during autotransplantation, a tear in the inferior vena cava (IVC) occurred leading to severe haemorrhage. A Gortex patch was sewn in the IVC, and circulation was maintained with 20 units of packed cells. Another patient experienced renal ischemia due to insufficient blood supply provided by a newly constructed aortorenal iliac graft and underwent a nephrectomy.

Post-operative complications

Post-operative management included intensive care admission for a median time of 1 (0–18) day after revascularisation procedures. Both hypotension and hypertension occurred for which intravenous inotropic drugs (n = 4) and labetalol and sodium nitroprusside (n = 15), respectively, were administered for a median duration of 2.5 days. A transient rise in plasma creatinine was observed in nearly all patients during the first week postoperatively. In all but one child plasma creatinine returned to baseline. One patient with bilateral RAS required renal replacement therapy with peritoneal dialysis for 1 month and emergency revascularisation of the contralateral kidney 4 weeks after an unplanned nephrectomy. In another patient, the split renal function deteriorated postoperatively from 55 to 5% secondary to renal ischemia after placement of an interposition graft. Chylous ascites was observed in one patient after bilateral renal surgery (autotransplantation and reimplantation of the renal artery) compromising renal function and requiring long-term oc-
treatment, medium-chain triglyceride feeds and eventually insertion of a peritoneo-venous shunt for adequate drainage. The shunt was removed 12 months later when the patient completely recovered.

Other complications were septicaemia \( (n = 5) \), pneumothorax secondary to a large haematoma \( (n = 1) \), haemothorax \( (n = 1) \) and abdominal haemorrhage \( (n = 4) \) causing secondary intestinal ischaemia in one patient and requiring surgical drainage in two children. Persistent feeding problems secondary to intestinal ischaemia occurred in one patient after implantation of an aortorenal graft. He was cured following stenting of the superior mesenteric artery, 18 days postoperatively.

Two secondary nephrectomies were performed 14 days and 7 months after saphenous vein graft insertion and splenorenal bypass surgery, respectively, as post-operative DMSA scans showed loss of function of the operated kidneys due to insufficient blood supply. There were no perioperative deaths, but two children died during follow-up (see long-term outcome paragraph).

**Short-term outcome**

All children benefited from a primary nephrectomy \( (n = 8 \) cured, \( n = 6 \) improved). Renal artery reimplantation was also successful with outcomes of cured \( (n = 2) \) and improved \( (n = 1) \). The majority of children benefited from a saphenous vein graft: cured \( (n = 1, 20\%) \), improved \( (n = 3, 60\%) \) and early technical failure \( (n = 1, 20\%) \).

A poor outcome was observed after autologous splenorenal bypass surgery with technical failure in four procedures due to loss of renal blood supply \( (n = 2) \) or re-stenosis of the bypass \( (n = 2) \).

Coexisting IRD, MAS or bilateral RAS was present in all patients who were not cured after surgery, and this was believed to be the reason for the need for continued treatment with antihypertensive drugs.

**Long-term outcome**

Two children died at median follow-up of 5.0 \((1.4–16.0)\) years for children living in the UK and 1 year for international referrals. The first patient died from a fatal haemorrhage due to a graft tear at 8 years of age after repeat angioplasty for a synthetic graft to a solitary kidney. Six years earlier, he had had an unplanned nephrectomy following the failure of revascularisation of the left kidney to the left internal iliac artery. The second patient died because of a major cerebral bleeding, at 18 years of age, 8 years after an aortorenal bypass with Gortex graft, multiple angioplasties and persistent hypertension secondary to intra-renal small vessel disease. One child was in end-stage renal failure, two had major behaviour problems, one had cerebral palsy and one had epilepsy. Eight children required 12 angioplasties for new lesions \( (n = 4) \) or technical failures \( (n = 8) \). One child developed a late stenosis of a saphenous vein graft.

SBP was cured in 18 \((49\%)\), improved in 14 \((38\%)\) or unchanged in five \((13\%)\). Normotension was achieved in 74 and 85\% of evaluated children at 1 year and at last follow-up, respectively, compared to 27% pre-operatively (Table 1). There was a major reduction of the need for antihypertensive drugs from a median of four to a median of one per each follow-up period (Table 1). It had been possible to stop all antihypertensive medications in 14 children, and only five children at 1 year follow-up and four children at last follow-up needed the same number of antihypertensive medicines as before the surgery.

eGFR was unchanged between surgery and the end of follow-up (Table 1). In only four patients did the eGFR decrease by more than 20\%, and one child needed chronic dialysis because of end-stage renal failure. Four patients developed proteinuria \((44 \ (19–225) \ mg/mmol)\) for which they received ACE inhibitors. Left ventricular hypertrophy was resolved in all patients.

**Discussion**

Our study shows that although surgery is not without risks, it is a feasible and potentially curative option in children with severe RVH, which is not controlled either by drugs or angioplasty. Eighty-seven percent of children in our cohort study population showed a benefit from the surgical procedure(s). It should be noted that children with RVH, unresponsive to a high number of antihypertensive drugs (and often an attempted angioplasty) who finally require a surgical procedure, are a complex group to manage. Generally, they showed an involvement of visceral arteries and/or coexisting cerebral disease and evidence of end-organ damage, predominantly left ventricular hypertrophy and kidney damage. Surgical treatment therefore represented an ultimate decision in a population of children at risk of major complications from their high BP (Table 3).

During the last 30 years, decisions regarding surgical intervention of RVH have changed. Angioplasty has become increasingly successful due to improved technology and increased experience with interventional radiology. We therefore recommend a stepwise approach to children with RVH with medical therapy as a first choice, angioplasty including stent angioplasty (where amenable) as a second choice and surgery reserved only for children in whom previous therapies have failed or in whom angioplasty is not possible due to the nature of the lesions (see suggested treatment pathway Figure 1). A team approach with paediatric nephrologists, interventional radiologists and surgeons is crucial.

In this cohort of children at high risk, the overall results of surgery, combined with angioplasty and medical treatment were quite good. Blood pressure responded to treatment in the majority of children with a major reduction of the need of antihypertensive treatment while renal function was maintained. There were a number of intra- and post-operative complications and of co-morbidities: two children died, one was in end stage renal disease, two had major behaviour problems, one had cerebral palsy and one had epilepsy. The long-term risks for these children would have been much higher if no surgical treatment would have been available.

The number of children who had had different operations in this study was too small to allow precise recommendations regarding the most appropriate surgical procedure. Traditionally, it has been our preference to pre-
form autologous surgery including autotransplantation, bypass surgery and insertion of autologous grafts over implantation of synthetic conduits when possible, as children, especially the younger children, could eventually outgrow these conduits. However, this approach was regarded as inappropriate in children with aortic or splanchnic artery involvement, as autologous surgery might compromise their collateral blood supply.

Renal revascularisation procedures with saphenous vein grafts were favoured during period I (1979–1988), although this procedure was abandoned after 1988 due to the literature reporting a high incidence of aneurysmal dilatation of the vein [21]. However, this did not occur in our cohort of patients. Between 1989 and 2000, splenorenal bypass surgery or insertion of aortorenal synthetic conduits was the treatment of choice. Since 2001, all children with RVH, potentially amendable to surgery, have undergone angioplasty before surgical correction of the lesion(s) was attempted. As a result, only the more challenging procedures have been performed including insertion of complex trouser grafts, combined renal artery and aortic reconstruction and aortic interposition grafts.

Surprisingly, we found a poor outcome after splenorenal, gastroduodenal-renal and iliorenal bypass surgery with a high incidence of failure due to early development of new stenotic disease in the inflow arteries or at the anastomosis. Additionally, complications and secondary nephrectomies accompanied both bypass procedures and autotransplantations. In contrast, children who underwent aortorenal saphenous vein grafts did quite well. Nevertheless, one early and one late technical failure accounted for a success rate of only 60% in this category. As expected, a favourable outcome was observed after bench reconstruction of renal arterial abnormalities and autotransplantation.

Our study represents one of the largest retrospective studies describing surgery in children with RVH. A recent report by Stanley and colleagues [9] describes excellent results of surgery in 97 children with RVH and represents the largest study so far. They describe a favourable outcome after implantation of the renal artery directly onto the aorta.

### Table 3. Outcome of surgery in our study population (n = 37)

<table>
<thead>
<tr>
<th>Primary surgery N=37</th>
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<tbody>
<tr>
<td>Unilateral procedure n=33</td>
</tr>
<tr>
<td>Bilateral procedures n=4</td>
</tr>
<tr>
<td>Cured</td>
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<tr>
<td>Improved</td>
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<td>Unchanged</td>
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<tr>
<td>Secondary surgery</td>
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<td>n=7</td>
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<table>
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<tr>
<th>Tertiary surgery n=2</th>
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<tbody>
<tr>
<td>Unilateral n=1</td>
</tr>
<tr>
<td>Bilateral n=1</td>
</tr>
<tr>
<td>Improved</td>
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<td>n=2</td>
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</table>
Proposed treatment pathway

Confirmed renovascular hypertension +/- mid-aortic syndrome and other vascular disease.

Treatment with antihypertensive drugs

Blood pressure well controlled

Blood pressure not well controlled

Angioplasty +/- stenting

Lesion not amenable to angioplasty +/- stenting

Surgery

Lesion not amenable to surgery

Blood pressure not well controlled

Blood pressure well controlled

Follow-up

Fig. 1. Proposed treatment pathway.

and after concomitant aortic and splanchnic artery reconstructions. The group avoids the use of aortorenal vein grafts due to the high incidence of aneurysmal dilatation [9,21,22]. Instead, the internal iliac artery is used in bench reconstructions, and in the majority of children, Dacron prosthetic bypass is used for aortorenal and aorto-aortic bypass. Additionally, they rarely perform splenorenal reconstructions since coeliac stenosis might develop later in life causing recurrent hypertension. Early graft stenoses after splenorenal bypasses have previously been reported [23]. Surgical approaches in children were prospectively studied by O'Neill in 50 children [15]. He reports a favourable outcome after using vein grafts that were wrapped by 6-mm Dacron mesh mandrills, preventing the vein grafts from aneurysmal degeneration.

Similar favourable outcomes, with no perioperative deaths, are reported in other recent series [24,25], in children and adolescents in whom RVH was caused by an heterogeneous group of lesions. In these series, nephrectomies were rarely performed, and renal artery repairs comprised bypasses (73% of 32 kidneys in 25 paediatric patients [24]) and arterial repairs (87% of 114 surgical procedures in 83 patients from 28 months to 18 years of age [25]).

Our surgical strategies have changed over time with less recourse to primary nephrectomy and extra-anatomic autologous bypass (hepato and splenorenal bypass). Complex segmental arterial reconstruction, direct renal arterial reimplantation and bilateral renal revascularisation together with aortic bypass in MAS using prosthetic bypass conduits are all safe and durable surgical interventions. Renal angioplasty even with the use of stents has not compromised subsequent surgery in our experience. This justifies our policy of keeping surgery as the last treatment option ideally in an older child with wider arteries and with the prospect of reducing the need for secondary procedures after the growth spurt of adolescence. In our experience, these surgical techniques, however, are also successful in smaller children and even babies as young as 4 months where angioplasty is not technically possible.

Children treated for RVH need lifelong follow-up (see suggested follow-up strategy). This needs to focus both on blood pressure, function of both kidneys and other involved vascular beds.

Conclusion

Surgery should be regarded as a relatively safe but later treatment option in children with severe RVH. We recommend renal artery reimplantation for children with RAS, insertion of a synthetic (trouser) graft in teenagers with (bilateral) RAS and coexisting involvement of their splanchnic bed. Nephrectomy should be reserved for a selected group of children with lesions that are not amendable
Renal artery revascularization improves HF control in patients with atherosclerotic RAS

Garvan C. Kane¹, Nancy Xu², Erik Mistrik³, Tomas Roubicek³, Anthony W. Stanson⁴ and Vesna D. Garovic²

¹Division of Cardiovascular Diseases, ²Division of Nephrology and Hypertension, Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA, ³Charles University, Hradec Karlove, Czech Republic and ⁴Department of Radiology, Mayo Clinic, Rochester, MN, USA

Correspondence and offprint requests to: Vesna D. Garovic; E-mail: garovic.vesna@mayo.edu

Abstract

Background. Renal artery stenosis (RAS) impacts the pathogenesis and control of heart failure (HF) and may further contribute to increased cardiovascular morbidity and mortality in HF patients. However, the long-term effects of renal artery revascularization on cardiovascular outcomes in HF patients are not well studied.

Methods. The prevalence of HF and its effects on all-cause mortality were studied in 163 consecutive patients with systemic hypertension and chronic kidney disease (serum...