PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Neonatal Renal Vein Thrombosis: Review of the English-Language Literature Between 1992 and 2006

Keith K. Lau, Jayson M. Stoffman, Suzane Williams, Patricia McCusker, Leonardo Brandao, Sanjay Patel and Anthony K.C. Chan

Pediatrics 2007;120;e1278
DOI: 10.1542/peds.2007-0510

REVIEW ARTICLE

Neonatal Renal Vein Thrombosis: Review of the English-Language Literature Between 1992 and 2006

Keith K. Lau, MD[a], Jayson M. Stoffman, MD[b], Suzane Williams, MD[c], Patricia McCusker, MD[b], Leonardo Brandao, MD[c], Sanjay Patel, MSc[d], Anthony K. C. Chan, MD[d], for the Canadian Pediatric Thrombosis and Hemostasis Network

[a]Department of Pediatrics, University of California, Davis, California; [b]Department of Pediatrics, University of Manitoba, Winnipeg, Manitoba, Canada; [c]Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada; [d]Division of Hematology/Oncology, Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

Renal vein thrombosis is a complication that occurs in neonates with various underlying risk factors. It carries a grave prognosis for affected kidneys. Anticoagulant and fibrinolytic therapies have been promoted in the past with anecdotal success in some circumstances. However, prospective controlled trials are still lacking, and to date there have been no evidence-based guidelines available for the treatment of neonates with renal vein thrombosis. We retrospectively reviewed all the available medical literature pertaining to renal vein thrombosis published in English during the past 15 years. A total of 271 patients from 13 case series were identified by using the terms "renal vein thrombosis" and "neonates" via PubMed and Cochrane Library searches. Data then were extracted from each of the studies for analysis. During the past 15 years, a male predominance (67.2%) in neonatal renal vein thrombosis has been reported. More than 70% of patients had unilateral renal vein thrombosis, which was more prevalent on the left side (63.6%). The thrombus involved the inferior vena cava and was associated with adrenal hemorrhage in 43.7% and 14.8% of neonates, respectively. Forty percent of the patients were treated conservatively with supportive care alone. Among those patients who received anticoagulation therapy, unfractionated heparin and low molecular weight heparin were used alone in 21.6% and 20.7% of the patients, respectively. Fibrinolytic treatment alone was used in 11.2% of the patients. Only a minority of patients were treated with antithrombin (1.7%), warfarin alone, (0.9%) or underwent surgical intervention (0.3%). The majority (70.6%) of the involved kidneys became atrophic. A total of 9 neonates died with non–renal vein thrombosis–related conditions during the study period. Evidence-based recommendations on treatment cannot be made at the present time. Cooperative prospective studies that involve multiple centers are needed to elucidate the optimal treatment for neonatal renal vein thrombosis.

www.pediatrics.org/cgi/doi/10.1542/peds.2007-0510

doi:10.1542/peds.2007-0510

Key Words
renal vein thrombosis, review, neonates

Abbreviations
RVT—renal vein thrombosis
LMWH—low molecular weight heparin

Accepted for publication Apr 24, 2007

Address correspondence to Anthony K. C. Chan, MD, McMaster University, Department of Pediatrics, Division of Hematology/Oncology, Room 3N27, 1200 Main St W, Hamilton, Ontario, Canada L8N 3Z5. E-mail: akchan@mcmaster.ca

THE EXACT INCIDENCE of renal vein thrombosis (RVT) in neonates is difficult to determine, because large-scale population-based epidemiologic studies are lacking. It has been reported to occur in 0.5 per 1000 admissions to NICUs according to a large international registry.[1] On the other hand, a recent study from Germany suggested that the incidence of symptomatic RVT in neonates was at least 2.2 per 100 000 live births.[2] Since the systematic and detailed review on the hemostatic complications of pediatric renal disease by Andrew and Brooker[3] more than 10 years ago, multiple case series and reports on neonates with RVT have been published. We reviewed the available English-language medical literature pertaining to neonatal RVT over the past 15 years to analyze and examine the data that are currently available on this neonatal disease. We intended to evaluate the efficacy of our current management strategies and identify potential improvement in the care of neonates with RVT.

METHODS

We searched the PubMed database from the National Library of Medicine using the keywords "renal vein thrombosis" and "neonates" with the limits set to only English-language articles and those that involved human subjects. An additional search was performed via the Cochrane Central Register of Controlled Trials and the Cochrane database of systemic reviews (Issue 4, 2006). We included all case reports and case series that were published in English from January 1992 to December 2006 that reported neonates with RVT. We excluded studies that contained discussion related to neonatal RVT but did not report on an actual case and those reports with 2 or fewer patients. Because the diagnostic criteria of RVT were not clearly stated in every study, we could not scrutinize the accuracy of the diagnosis of each reported case.

Data were extracted from individual studies onto a spreadsheet (Excel; Microsoft, Redmond, WA) for additional analysis. Because the design and methodologies used varied among the studies, some did not have all the information that we intended to analyze. Data are included in the analysis if they were actually described in the study; if a test was not mentioned in the study, the result was entered as unknown.

RESULTS

The search strategies identified 77 publications; 64 were excluded from analysis. Thirty-seven of those reports were excluded because the number of cases included were 2 or fewer.[4–40] One case series, reported by the 1-800-NO-CLOTS registry,[41] was also excluded from the study because of the potential overlap of patients from other reported cases. Another case series of 23 children with RVT was also excluded[42] because 4 of the patients presented after the neonatal period but could not be removed from the aggregate analysis. As a result, a total of 13 case series were included for analysis.[1,2,43–53] All of the reported cases had objective documentation of RVT from ultrasound.

Patient Characteristics

Table 1 describes the studies that were included in our review. A total of 271 neonates were included, with a male predominance (67.2% [127 of 189]). Figure 1 depicts the time of onset of RVT. Although all the patients were diagnosed to have RVT within the first month of life, detailed information on the exact time of disease onset was not available from all studies. However, data compiled from studies with that information show that 7.3% (6 of 82), 67.1% (55 of 82), and 25.6% (21 of 82) of the neonates presented in utero, within 3 days, and more than 3 days after birth, respectively. Most of the patients were born at term (71.3% [97 of 136]).

Presentation

Of the neonates, 70.3% (173 of 246) had unilateral RVT; 63.6% (63 of 99) of these cases involved the left kidney.

TABLE 1 **Studies in the English-Language Literature That Had Reported Cases (≥3) of Neonatal RVT**

Author (Year)	*n*	F	M	Unilateral	Bilateral	L	R
Messinger et al[43] (2006)	28	8	20	25	3	15	10
Winyard et al[44] (2006)	23	6	17	10	13	7	3
Marks et al[45] (2005)	43	15	28	24	19	NA	NA
Proesmans et al[46] (2005)	5	1	4	3	2	2	1
Kosch et al[47] (2004)	59	24	35	43	16	23	20
Heller et al[48] (2000)	25	NA	NA	NA	NA	NA	NA
Bökenkamp et al[2] (2000)	35	NA	NA	28	7	NA	NA
Schmidt and Andrew[1] (1995)	21	5	16	18	3	NA	NA
Keiden et al[49] (1994)	6	2	4	5	1	5	0
Nuss et al[50] (1994)	6	NA	NA	3	3	1	2
Laplante et al[51] (1993)	8	NA	NA	7	1	7	0
Orazi et al[52] (1993)	4	1	3	3	1	3	0
Nowak-Göttl et al[53] (1992)	8	NA	NA	4	4	NA	NA
Total	271	62	127	173	73	63	36

F indicates female; M, male; L, left kidney; R, right kidney; NA, not applicable.

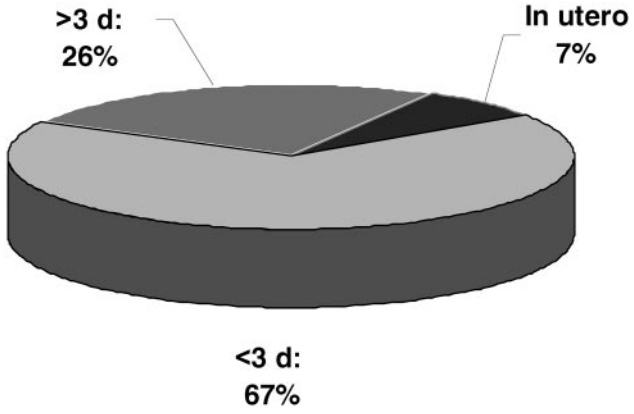

FIGURE 1
Age at onset of RVT.

Figure 2 depicts the features of the patients at presentation. The thrombus extended into the inferior vena cava in 43.7% (90 of 206) of the patients. Adrenal hemorrhage was present in 14.8% (31 of 210) of the patients. Because most of the patients were reported as case series rather than as individual cases, individual clinical features at presentation could not be analyzed and correlated with outcomes. Perinatal risk factors including asphyxia were identified in 31.9% (69 of 216) of the reported cases. Other known risk factors such as maternal diabetes mellitus and dehydration were reported in 8.1% (17 of 210) and 1.5% (3 of 206) of the patients, respectively. Although all the patients had ultrasound-documented RVT, most of them also had at least 1 of the 3 cardinal signs of RVT at presentation: 56.2% (73 of 130) had macroscopic hematuria, 45.4% (83 of 183) had a palpable abdominal mass, and 47.5% (85 of 179) had thrombocytopenia.

Prothrombotic Risk Factors

Not all of the studies collected data on their patients' prothrombotic risks. Before 1996, the only prothrombotic abnormality reported was the presence of the lupus anticoagulant. Since that time, other prothrombotic factors, including protein C, protein S, plasma antithrombin III activity, lipoprotein(a), factor V Leiden mutation, prothrombin gene mutation, and methylenetetrahydrofolate (*MTHFR*) thermolabile mutation have also been screened in some studies. Among patients with RVT in whom prothrombotic factors were investigated, 53% (79 of 149) had at least 1 risk factor identified. The recurrence rate of thromboembolic events was reported in 1 study.[47] With a median follow-up time of 4 years (range: 0.6–15 years), 6.8% (4 of 59) of the patients with RVT had a second thrombotic event, occurring during puberty in 3 of the 4 patients. All 4 patients had at least 1 prothrombotic risk factor.

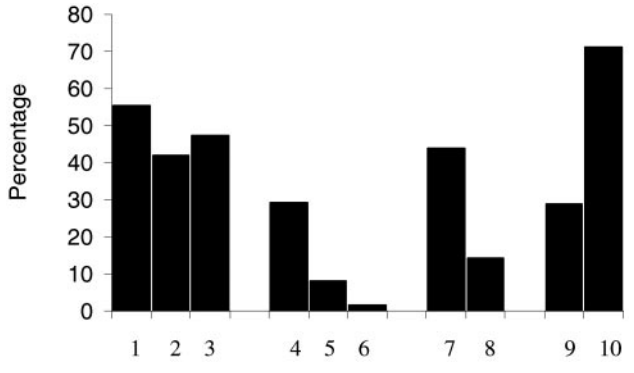

FIGURE 2
Features at presentation: 1, macroscopic hematuria (55.4%); 2, palpable mass (42.1%); 3, thrombocytopenia (47.5%); 4, perinatal asphyxia (29.2%); 5, maternal diabetes mellitus (8.1%); 6, dehydration (1.5%); 7, thrombus extended into inferior vena cava (43.7%); 8, adrenal hemorrhage (14.3%); 9, gestational age of <36 weeks (28.7%); 10, gestational age of >36 weeks (71.3%).

Treatment Modalities

Ten of the 13 studies reviewed contained data on treatment of RVT. Figure 3 illustrates the different treatment modalities that the patients received: 39.7% (92 of 232) received supportive therapy alone, and 21.6% (50 of 232) and 20.7% (48 of 232) of the patients received unfractionated heparin or low molecular weight heparin (LMWH) alone, respectively. Slightly more than 11% (11.2% [26 of 232]) were given fibrinolytic treatment. A small minority of patients were managed with antithrombin (1.7% [4 of 232]) or warfarin (0.9% [2 of 232]) alone or surgical interventions (0.3% [9 of 232]). Approximately 4% (3.9% [9 of 232]) of the patients received combinations of treatment that included heparin, fibrinolytic agents, warfarin, and protein C concentrate.

Outcomes

Renal outcomes were not reported consistently in the studies. Regardless of the treatment received, irreversible damage was found in 70.6% (156 of 221) of the affected kidneys at last follow-up. In patients treated with unfractionated heparin/LMWH or supportive care, 75.3% (61 of 81) and 72.5% (45 of 62), respectively, of the affected kidneys were found to be atrophic at last follow-up (Table 2). Although the definitions used for

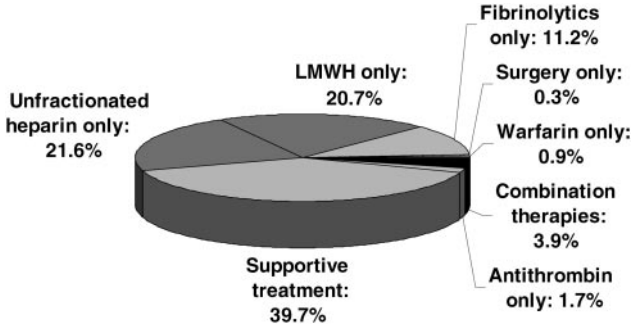

FIGURE 3
Treatment modalities of the neonates with RVT.

TABLE 2 **Studies in the English-Language Literature That Had Reported the Incidence of Kidney Atrophy in Heparin-Treated or Supportively Managed Neonates With RVT**

Author (Year)	Heparin Treated	Supportive Only
Messinger et al[43] (2006)	4 (10)	9 (16)
Winyard et al[44] (2006)	4 (4)	13 (19)
Kosch et al[47] (2004)	30 (33)	10 (11)
Bökenkamp et al[2] (2000)	18 (26)	5 (8)
Keiden et al[49] (1994)	2 (2)	4 (4)
Nuss et al[50] (1994)	3 (6)	0 (0)
Orazi et al[52] (1993)	0 (0)	4 (4)
Total	61 (81)	45 (62)

The incidence is shown as number of neonates with atrophic kidneys and the total number of patients treated in parentheses.

chronic renal insufficiency were heterogeneous and often unspecified, 8 neonates (3.0% [8 of 271]) required chronic renal replacement therapies and renal transplantations. Four of these 8 neonates had bilateral RVT; the extent was not documented for the other 4 patients.

Seven of the 13 studies provided follow-up information for hypertension: 19.3% (27 of 140) of the patients had persistent elevation of blood pressure. Laterality of the involved kidneys was provided for 120 patients: 18.9% (14 of 74) of the neonates with unilateral RVT and 21.7% (10 of 46) of the neonates with bilateral RVT had persistent elevated blood pressure (Table 3).

A total of 9 deaths were reported, all of which were related to coexisting medical conditions such as respiratory failure in 3 neonates, multiorgan failure in 1 neonate, and sepsis/meningitis in another neonate. The cause of death of the other neonates was not provided by the authors of the report.

DISCUSSION

RVT is the most common non–catheter-related thrombosis in infancy and occurs primarily in the newborn period.[3] Although many reviews of RVT can be identified in the literature, evidence-based management guidelines are still lacking. In this study, we retrospectively analyzed all the available case series with more than 2 patients on neonatal RVT published in English over the last 15 years. Our intent was to gather the accumulated experience from different sources, evaluate the current management strategies for neonatal RVT, and provide direction for future research in this important hemostatic disorder in neonates.

TABLE 3 **Studies in the English-Language Literature That Had Reported the Incidence of Hypertension at Last Follow up in Neonates With Unilateral and Bilateral RVT**

Author (Year)	Unilateral	Bilateral	Nonspecified
Winyard et al[44] (2006)	1 (10)	3 (13)	—
Marks et al[45] (2005)	1 (10)	2 (12)	—
Kosch et al[47] (2004)	10 (43)	3 (16)	—
Bökenkamp et al[2] (2000)	—	—	3 (20)
Keiden et al[49] (1994)	0 (5)	0 (1)	—
Nuss et al[50] (1994)	0 (3)	0 (1)	—
Orazi et al[52] (1993)	2 (3)	0 (1)	—
Total	14 (74)	10 (46)	—

The incidence is shown as number of neonates with elevated blood pressure and the total number of patients with unilateral or bilateral RVT in parentheses. — indicates that data were not available.

In an earlier review that included 268 children with RVT, of which 212 were neonates, the incidence in boys and girls was similar and the left and right sides were affected equally.[3] Other studies have noted a male predominance, as we have observed in this review. It is uncertain whether this represents a changing demographic of RVT. In our study, the incidence of bilateral RVT was 29.7%, compared with 24% in the earlier review. Preterm infants have been considered to be at risk of developing RVT, and we found that 28.7% of the affected neonates were born before 36 weeks of gestation. Although the classical "triad" of RVT (macroscopic hematuria, palpable abdominal mass, and thrombocytopenia) has been well described, these 3 elements are not always found at presentation. Winyard et al[44] recently showed that only 23.5% (5 of 21) of their neonates had the triad at presentation. Perinatal asphyxia, dehydration, and maternal diabetes mellitus are established risk factors for RVT. However, we found that less than one third of the affected neonates had a history of perinatal asphyxia, and dehydration and maternal diabetes mellitus were even less common.

Hereditary prothrombotic risk factors may also play a role in the pathogenesis of neonatal RVT, and routine screening for known procoagulant abnormalities has been suggested.[24,45] We found that 53% (79 of 149) of the patients who had been investigated were found to have 1 or more prothrombotic risk factors. In a recent study of 301 children with various types of spontaneous thromboembolism, 21.3% of the patients experienced a recurrence at a median of 3.5 years after cessation of prophylaxis.[54] Among those children whose symptoms recurred, 48.4% had a single prothrombotic risk factor and 46.9% had 2 or more risk factors. The authors concluded, therefore, that it is reasonable to screen children with symptomatic thromboembolic diseases for prothrombotic risk factors. However, 1 study in our review[47] found that only 6.8% (4 of 59) of the affected neonates had a recurrence of thrombosis, and 3 of the 4 patients had the recurrence during puberty. Another study did not find any recurrence of the thrombosis beyond the neonatal period in neonates with prothrombotic risk factor at a median follow-up of 3.7 years (range: 0.5–20.2 years).[45] Because there are no data to indicate that routine screening in neonates with RVT reduces the recurrence risk, there is no evidence to support routine screening for prothrombotic risk factors in neonates with RVT.

Ultrasound is a useful and convenient clinical tool for

the diagnosis of RVT. Sonographic features of RVT include enlarged and echogenic kidneys with attenuation or loss of corticomedullary differentiation. Calcification and thrombus may be seen extending outside the kidneys to the inferior vena cava. Ultrasound may also be of prognostic significance for RVT. Winyard et al[44] reported a negative correlation between renal length and renal outcomes. Doppler studies are particularly useful for detecting the resistance or absence of flow in renal venous branches and collateral vessels. Although the blood flow in the main renal vein and its branches may be normal, there may be an increase in resistance in the renal arteries caused by thrombosis in the small intrarenal veins. Renal scarring and atrophy are well-recognized features after RVT in affected kidneys, which can also be assessed by a radionuclide scan.

Heparin therapy has been proposed for neonates with RVT, especially in those with bilateral RVT and with inferior vena cava involvement.[3] Recently, the trend has been toward the use of LMWH rather than unfractionated heparin. However, almost 40% of the affected neonates were managed by supportive care alone. Our data show that the treatment of neonates with RVT varies greatly among centers, and evidence-based recommendations on this practice are not available. The data suggest that the renal outcomes were similar between supportive treatment and heparin therapies, and a similar proportion of affected kidneys became atrophic in neonates who were managed supportively or with heparin. RVT in neonates often leads to irreversible damage, and anticoagulant therapies may not have an impact on the long-term outcomes.

Although there is no consensus on the management of neonatal RVT, the management should involve a multidisciplinary team that includes neonatologists, radiologists, hematologists, and nephrologists. During the acute phase, supportive management of electrolytes and fluid balance with input from the nephrologists is essential, particularly if the neonates are in acute renal failure and require renal replacement therapies. The hematologists should be consulted on whether and when the neonates require anticoagulation or fibrinolytic treatments. The response to the treatment should be monitored by the clinical team in conjunction with the radiologists and ultrasonographers.

Affected neonates must be followed closely for renal complications such as hypertension, atrophy, functional loss, and chronic renal insufficiency. In our review, reporting on outcomes of the affected neonates was incomplete in many of the publications; the length of follow-up and definitions for chronic kidney diseases were also variable. Persistent hypertension was reported in one fifth of the neonates, and 8 neonates (3.0%) were reported to need chronic dialysis or kidney transplantation. Because of the heterogeneity of treatment approaches and outcome measures, we are not able to draw any conclusion on the impact of different treatment strategies on long-term outcomes.

Nine deaths were reported, and all were non–RVT related. The mortality rate in children with thromboembolic disease from all causes was reported as 5% in a large international registry[1] that was published more than 10 years ago. The mortality rate of neonates with RVT that we observed in our study was 3.3% (9 of 271).

Although we retrospectively pooled the available data on neonates with RVT over the last 15 years from multiple centers, we still cannot make any evidence-based recommendations for current treatment strategies. Randomized, controlled trials may not be feasible because of the low incidence of RVT and limited patient numbers in individual centers. However, a prospective multicenter trial with standardized protocols for treatment and long-term follow-up of neonatal RVT should be possible and practical.

CONCLUSIONS

Our study illustrates the variability of treatment strategies for neonates with RVT and, potentially, a change in demographics of this condition. Renal outcomes of the affected kidneys are still unsatisfactory for the majority of neonates with RVT. Evidence-based recommendations for the optimal treatment of neonatal RVT are not possible, but prospective multicenter trials with standardized protocols are feasible and should be undertaken as soon as possible to identify the most appropriate treatment strategies for neonates with RVT.

REFERENCES

1. Schmidt B, Andrew M. Neonatal thrombosis: report of a prospective Canadian and international registry. *Pediatrics.* 1995; 96:939–943
2. Bökenkamp A, von Kries R, Nowak-Göttl U, Göbel U, Hoyer PF. Neonatal renal venous thrombosis in Germany between 1992 and 1994: epidemiology, treatment and outcome. *Eur J Pediatr.* 2000;159:44–48
3. Andrew M, Brooker LA. Hemostatic complications in renal disorders of the young. *Pediatr Nephrol.* 1996;10:88–99
4. Prelog M, Fischer H, Gassner I, et al. Bilateral renal vein thrombosis in a twin newborn without known risk factors. *Clin Nephrol.* 2006;66:135–139
5. Kobayashi T, Kobayashi T, Mayuzumi H, Morikawa A. Percutaneous hydrodynamic thrombectomy for congenital deep vein thrombosis in a neonate. *Pediatr Cardiol.* 2006;27:170–174
6. Shafagh H, Soltani MA, Douvoyiannis M, et al. Index of suspicion. *Pediatr Rev.* 2005;26:461–466
7. Anochie IC, Eke F. Renal vein thrombosis in the neonate: a case report and review of the literature. *J Natl Med Assoc.* 2004;96:1648–1652
8. Argyropoulou MI, Giapros VI, Papadopoulou F, et al. Renal venous thrombosis in an infant with predisposing thrombotic factors: color Doppler ultrasound and MR evaluation. *Eur Radiol.* 2003;13:2027–2030
9. Lee CH. Intestinal obstruction caused by infarcted splenic hemangioma with renal vein thrombosis in a newborn: a case report. *Int Surg.* 2002;87:157–159
10. Weinschenk N, Pelidis M, Fiascone J. Combination thrombo-

lytic and anticoagulant therapy for bilateral renal vein thrombosis in a premature infant. *Am J Perinatol.* 2001;18:293–297
11. Giordano P, Laforgia N, Di Giulio G, Storelli S, Mautone A, Iolascon A. Renal vein thrombosis in a newborn with prothrombotic genetic risk factors. *J Perinat Med.* 2001;29:163–166
12. Wilkinson AG, Murphy AV, Stewart G. Renal venous thrombosis with calcification and preservation of renal function. *Pediatr Radiol.* 2001;31:140–143
13. Wheeler DS, Poss WB, Stocks AL. Radiological case of the month: inferior vena cava and renal vein thrombosis in a neonate. *Arch Pediatr Adolesc Med.* 2001;155:415–416
14. Suga K, Hara A, Motoyama K, Ishikawa Y, Kume N, Matsunaga N. Coexisting renal vein thrombosis and bilateral adrenal hemorrhage: renoscintigraphic demonstration. *Clin Nucl Med.* 2000;25:263–267
15. Anguenot JL. Antenatal renal vein thrombosis after accidental electric shock in a pregnant woman. *J Ultrasound Med.* 1999;18:779–781
16. Izquierdo V, Gómez D, Macías E, et al. Tc-99m MAG3 scintigraphy in a newborn with acute renal vein thrombosis. *Clin Nucl Med.* 1999;24:287–288
17. Klinge J, Scharf J, Rupprecht T, Boswald M, Hofbeck M. Selective thrombolysis in a newborn with bilateral renal venous and cerebral thrombosis and heterozygous APC resistance. *Nephrol Dial Transplant.* 1998;13:3205–3207
18. Schild RL, Lobb MO, Voke JM. Hereditary thrombophilia in a family with three independent protein S and C mutations: a cause of adverse perinatal outcome. *Eur J Obstet Gynecol Reprod Biol.* 1998;80:283–285
19. Navarro O, Daneman A, Kooh SW. Asymmetric medullary nephrocalcinosis in two children. *Pediatr Radiol.* 1998;28:687–690
20. Diallo AB, Boog GJ, Moussally F, Quere MP, Roze JC. Renal venous thrombosis: an unusual cause of fetal distress. *Eur J Obstet Gynecol Reprod Biol.* 1998;79:109–113
21. Lash C, Radhakrishnan J, McFadden JC. Renal vein thrombosis secondary to absent inferior vena cava. *Urology.* 1998;51:829–830
22. Pohl M, Zimmerhackl LB, Heinen F, Sutor AH, Schneppenheim R, Brandis M. Bilateral renal vein thrombosis and venous sinus thrombosis in a neonate with factor V mutation (FV Leiden). *J Pediatr.* 1998;132:159–161
23. Cozzolino DJ, Cendron M. Bilateral renal vein thrombosis in a newborn: a case of prenatal renal vein thrombosis. *Urology.* 1997;50:128–131
24. Haffner D, Wuhl E, Zieger B, Grulich-Henn J, Mehls O, Schaefer F. Bilateral renal venous thrombosis in a neonate associated with resistance to activated protein C. *Pediatr Nephrol.* 1996;10:737–739
25. Wright NB, Blanch G, Walkinshaw S, Pilling DW. Antenatal and neonatal renal vein thrombosis: new ultrasonic features with high frequency transducers. *Pediatr Radiol.* 1996;26:686–689
26. Formstone CJ, Hallam PJ, Tuddenham EG, et al. Severe perinatal thrombosis in double and triple heterozygous offspring of a family segregating two independent protein S mutations and a protein C mutation. *Blood.* 1996;87:3731–3737
27. Kumar A, Chaudhary D, Bhargava V. Recovery from bilateral renal vein thrombosis on supportive management alone. *Indian J Pediatr.* 1995;62:251–252
28. Errington ML, Hendry GM. The rare association of right adrenal haemorrhage and renal vein thrombosis diagnosed with duplex ultrasound. *Pediatr Radiol.* 1995;25:157–158
29. Lin GJ, Yang PH, Wang ML. Neonatal renal venous thrombosis: a case report describing serial sonographic changes. *Pediatr Nephrol.* 1994;8:589–591
30. Loges RJ, Tulchinsky M, Boal DK, Tulli MA, Eggli DF. Tc-99m MAG3 renography in renal vein thrombosis secondary to Finnish-type congenital nephrotic syndrome. *Clin Nucl Med.* 1994;19:888–891
31. Hage ML, Liu R, Marcheschi DG, Bowie JD, Allen NB, Macik BG. Fetal renal vein thrombosis, hydrops fetalis, and maternal lupus anticoagulant: a case report. *Prenat Diagn.* 1994;14:873–877
32. Tran-Minh VA, Genin G, Pracros JP, Foray P, Bourgeois J. Coexisting calcified inferior vena cava thrombus and adrenal hemorrhage in the neonate: report of three cases. *J Clin Ultrasound.* 1994;22:103–108
33. Fishman JE, Joseph RC. Renal vein thrombosis in utero: duplex sonography in diagnosis and follow-up. *Pediatr Radiol.* 1994;24:135–136
34. Dillon PW, Fox PS, Berg CJ, Cardella JF, Krummel TM. Recombinant tissue plasminogen activator for neonatal and pediatric vascular thrombolytic therapy. *J Pediatr Surg.* 1993;28:1264–1268
35. Alexander AA, Merton DA, Mitchell DG, Gottlieb RP, Feld RI. Rapid diagnosis of neonatal renal vein thrombosis using color Doppler imaging. *J Clin Ultrasound.* 1993;21:468–471
36. Herman TE, Siegel MJ. Special imaging casebook: neonatal adrenal hemorrhage and renal vein thrombosis. *J Perinatol.* 1993;13:325–328
37. Lund PJ, Seeds JW. Case of the day: renal vein and inferior vena cava thrombosis in a newborn. *J Ultrasound Med.* 1993;12:248
38. Rypens F, Avni F, Braude P, et al. Calcified inferior vena cava thrombus in a fetus: perinatal imaging. *J Ultrasound Med.* 1993;12:55–58
39. Contractor S, Hiatt M, Kosmin M, Kim HC. Neonatal thrombosis with anticardiolipin antibody in baby and mother. *Am J Perinatol.* 1992;9:409–410
40. Veiga PA, Springate JE, Brody AS, Cummings JJ, Mosovich L, Feld LG. Coexistence of renal vein thrombosis and adrenal hemorrhage in two newborns. *Clin Pediatr (Phila).* 1992;31:174–176
41. Kuhle S, Massicotte P, Chan A, Mitchell L. A case series of 72 neonates with renal vein thrombosis: data from the 1–800-NO-CLOTS registry. *Thromb Haemost.* 2004;92:729–733
42. Zigman A, Yazbeck S, Emil S, Nguyen L. Renal vein thrombosis: a 10-year review. *J Pediatr Surg.* 2000;35:1540–1542
43. Messinger Y, Sheaffer JW, Mrozek J, Smith CM, Sinaiko AR. Renal outcome of neonatal renal venous thrombosis: review of 28 patients and effectiveness of fibrinolytics and heparin in 10 patients. *Pediatrics.* 2006;118(5). Available at: www.pediatrics.org/cgi/content/full/118/5/e1478
44. Winyard PJ, Bharucha T, De Bruyn R, et al. Perinatal renal venous thrombosis: presenting renal length predicts outcome. *Arch Dis Child Fetal Neonatal Ed.* 2006;91:F273–F278
45. Marks SD, Massicotte MP, Steele BT, et al. Neonatal renal venous thrombosis: clinical outcomes and prevalence of prothrombotic disorders. *J Pediatr.* 2005;146:811–816
46. Proesmans W, van de Wijdeven P, Van Geet C. Thrombophilia in neonatal renal venous and arterial thrombosis. *Pediatr Nephrol.* 2005;20:241–242
47. Kosch A, Kuwertz-Broking E, Heller C, Kurnik K, Schobess R, Nowak-Göttl U. Renal venous thrombosis in neonates: prothrombotic risk factors and long-term follow-up. *Blood.* 2004;104:1356–1360
48. Heller C, Schobess R, Kurnik K, et al. Abdominal venous thrombosis in neonates and infants: role of prothrombotic risk factors—a multicentre case-control study. For the Childhood Thrombophilia Study Group. *Br J Haematol.* 2000;111:534–539
49. Keidan I, Lotan D, Gazit G, Boichis H, Reichman B, Linder N. Early neonatal renal venous thrombosis: long-term outcome. *Acta Paediatr.* 1994;83:1225–1227

50. Nuss R, Hays T, Manco-Johnson M. Efficacy and safety of heparin anticoagulation for neonatal renal vein thrombosis. *Am J Pediatr Hematol Oncol.* 1994;16:127–131
51. Laplante S, Patriquin HB, Robitaille P, Filiatrault D, Grignon A, Décarie JC. Renal vein thrombosis in children: evidence of early flow recovery with Doppler US. *Radiology.* 1993;189:37–42
52. Orazi C, Fariello G, Malena S, Schingo P, Ferro F, Bagolan P. Renal vein thrombosis and adrenal hemorrhage in the newborn: ultrasound evaluation of 4 cases. *J Clin Ultrasound.* 1993; 21:163–169
53. Nowak-Göttl U, Schwabe D, Schneider W, Schlosser R, Kreuz W. Thrombolysis with recombinant tissue-type plasminogen activator in renal venous thrombosis in infancy. *Lancet.* 1992;340:1105
54. Nowak-Göttl U, Junker R, Kreuz W, et al. Risk of recurrent venous thrombosis in children with combined prothrombotic risk factors. *Blood.* 2001;97:858–862

Neonatal Renal Vein Thrombosis: Review of the English-Language Literature Between 1992 and 2006

Keith K. Lau, Jayson M. Stoffman, Suzane Williams, Patricia McCusker, Leonardo Brandao, Sanjay Patel and Anthony K.C. Chan

Pediatrics 2007;120;e1278
DOI: 10.1542/peds.2007-0510