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Michael Riccabona
Ekkehard Ring
Wolfgang Schwinger
Reingard Aigner

Amplitude coded-colour Doppler sonography in paediatric renal disease

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M. Riccabona (✉)
Department of Radiology,
Division of Paediatric Radiology,
University Hospital LKH Graz,
Auenbruggenplatz,
8036 Graz, Austria
e-mail: michael.riccabona@kfunigraz.ac.at
Tel.: + 31-6-3 85 42 03;
Fax: + 31–6-3854299

R. Aigner
Department of Radiology,
Division of Nuclear Medicine,
University Hospital LKH Graz,
Auenbruggenplatz,
8036 Graz, Austria

E. Ring
Department of Paediatrics,
Division of General Paediatrics,
University Hospital LKH Graz,
Auenbruggenplatz,
8036 Graz, Austria

W. Schwinger
Department of Paediatrics,
Division of Paediatric Oncology,
University Hospital LKH Graz,
Auenbruggenplatz,
8036 Graz, Austria

Abstract The aim of our study was to assess the ability of amplitude coded-colour Doppler sonography (ACDS) to depict altered perfusion in paediatric renal disease in a prospective study. Colour Doppler sonography (CDS) and ACDS examinations were performed in 180 renal units (90 patients; age range newborn to 16 years) with unilateral or bilateral renal disease (e. g. reflux nephropathy, renal scars, end-stage renal disease, ureteropelvic junction obstruction, urinary tract infection, renal failure, haemolytic uraemic syndrome, nephrotic syndrome, systemic lupus erythematosus (LE), renal biopsy, congenital dysplasia, tumour/infiltration). The ACDS results were compared with scintigraphy or CT as well as to clinical findings. Amplitude colour-coded Doppler sonography accurately demonstrated normal vasculature in 49 of 51 healthy kidneys (= 96 %); 3 healthy kidneys could not be evaluated due to motion/artefacts. In 39 of 43 kidneys with focally altered perfusion ACDS could be performed and correctly depicted focally impaired vasculature/perfusion in 35 kidneys (= 89.7 %). Seventy-three of 83 kidneys with diffusely impaired perfusion could be evaluated by ACDS and altered pattern was correctly depicted in 58 kidneys (= 79.4 %), with an overall percentage of agreement of 87.1 %. Amplitude CDS appears to be useful in infants and children. Compared with CDS it improves visualisation of especially focally impaired vasculature/perfusion and should be considered a valuable adjunct to conventional investigations.

Key words Kidney · Colour Doppler · sonography · Colour Doppler energy · Power Doppler · Infants · Paediatrics

Introduction

Recently, amplitude-coded colour Doppler sonography (ACDS) also called power Doppler or colour Doppler energy, was introduced to medical imaging. This new Doppler technique relies on the totally integrated Doppler spectrum creating a signal with uniform low background noise, thus achieving higher gains without being obscured by noise [1, 2, 3]. This results in a higher sensitivity to low flow. Amplitude CDS depicts the number of moving cells, in addition to flow velocity, and is more equivalent to flow volume [2, 4]. It reduces angle dependency, but also increases the risk of "flash" artefacts from patient movements or breathing. Particularly in

adults ACDS has already become an established modality in demonstrating organ perfusion [4, 5, 6, 7].

Renal disease may involve renal vessels and may affect renal perfusion. The value of conventional colour Doppler sonography (CDS) has already been established in the diagnosis of paediatric nephrological/urological conditions, e.g. in evaluating perfusion of obstructed kidneys, cystic renal disease, renal artery stenosis, renal vein thrombosis and renal transplants [8, 9, 10, 11, 12]. The kidney represents a highly vascularised organ ideal for ACDS applications. Initial results in small series have shown that diminished perfusion may be reliably detected by ACDS; first reports have suggested that ACDS may be of value in paediatric renal disease [13, 14, 15, 16, 17, 18, 19, 20].

The aim of this prospective study was to evaluate the use of ACDS in paediatric nephrological/urological conditions in children with diffuse or focally altered renal perfusion/vasculature as compared with conventional CDS and with the final diagnosis.

Patients and methods

Ninety patients with an average age of 7.2 years (age range newborn to 16 years, male:female = 41:49, 14 neonates and infants, 31 children between 3 and 6 years, 35 children aged 7–10 years, 10 children and youngsters older than 10 years) were scanned and included in this prospective study. Twenty-six patients had reflux nephropathy (RNP) and renal scars including end-stage renal disease, and 24 patients had uretero-pelvic junction obstruction (UPJO). Renal parenchymal involvement/disease of various causes, such as urinary tract infection, renal failure, haemolytic uraemic syndrome, nephrotic syndrome and systemic lupus erythematosus (LE), was present in 19 patients; 8 patients suffered from renal cystic disease. Thirteen patients had various "other conditions" such as before/after renal biopsy, severe congenital dysplasia or tumour/infiltration. Renal transplants were excluded from this study to prevent bias by significantly easier sonographic access with fewer motion-induced ACDS artefacts.

Ultrasound was performed using an Acuson 128 XP 10 or Sequoia 512 Ultrasound device (Acuson, Mountain View, Calif.) with various multifrequency transducers (8 to 3.5 MHz). Conventional CDS was performed initially, ACDS was then applied with manipulation of colour gain until colour noise became apparent. Gate, filter, scale and persistence were optimised keeping the focus zone in the centre of the colour box. In each patient both kidneys were assessed, using the healthy kidney (in patients with unilateral disease as confirmed by other imaging methods) for comparison. In patients with bilateral disease the spleen was used as an intra-individual gold standard. In all kidneys the largest amount of depictable vasculature throughout the whole kidney was assessed in either prone or supine position (whichever was optimal for visualisation). Since ACDS was considered an approved technique, no informed consent had to be obtained for these studies.

No patient was sedated. Special manoeuvres, such as breath-holding, were performed in older patients capable of cooperation.

All investigations were performed by the same radiologist. Repeated studies during the course of the disease as well as duplex Doppler velocity measurements and inter-/intra-observer variability were not evaluated.

Excluding the 18 patients seen for renal biopsy, with tumours, at the intensive care unit, or with nephrotic syndrome, all other 72 patients underwent static scintigraphy using 30–60 MBq 99 m Tc DMSA and posterior acquisition. A nuclear medicine specialist independently interpreted the images.

Depending on the clinical situation and suspected underlying disease, further imaging was performed. This included voiding cystourethrography and/or intravenous pyelography (IVP) in 70 patients with urinary tract malformation, reflux nephropathy, and/or urinary tract infection as well as with dysplastic kidneys and cystic renal disease. Furthermore, multiphasic contrast-enhanced spiral CT was performed in 7 patients with suspicion of tumour; in 4 of them MR imaging and angiography were performed additionally. These reference studies were performed within 48 h of the ACDS examination, either before or after, except for patients with scars: in these patients scintigraphy was performed within 1 week before or after US examination.

Clinical and laboratory findings, such as blood count, C-reactive protein, urine sample and urine culture, and serological findings, such as CMV titer and renal functional parameters, were available. Histological results were obtained in patients with tumours or with renal biopsies. These data were only used for establishing the final diagnosis but were not implemented in the work-up of ACDS findings. In patients with unilateral disease the other kidney – even with compensatory hypertrophy – was considered normal on the base of normal IVP, conventional ultrasound and scintigraphy.

The results of ACDS regarding the demonstration of focal or diffuse changes in renal perfusion/vasculature were evaluated and compared with the results of CDS, scintigraphy and the other imaging methods (IVP, CT and MRI, when available), and, when available, with the results of histology and clinical data (e.g. in acute renal failure, laboratory data on renal involvement in urinary tract infection). The ACDS readings were performed immediately after the investigation and the reader was blinded to the results of other imaging modalities. The degree to which ACDS provided additional diagnostic information was assessed by comparison with CDS studies.

For statistical analysis, three groups were established: a group with normal kidneys (group 0), group 1 with focally altered perfusion and group 2 with diffusely impaired perfusion. Since sensitivity and specificity could not be calculated due to some missing data in each subgroup, such as some non-diagnostic ACDS examinations in each subgroup, only accuracy (i.e. percentage of agreement) was calculated.

Results

A total of 180 kidneys with 126 abnormal renal units were investigated. In 54 patients with unilateral disease the involved and uninvolved kidneys were compared; 36

Fig. 3 a, b Amplitude CDS of diffusely altered renal perfusion. ▶ **a** Demonstration of rarefaction of colour-coded vessels, especially peripherally, in relation to normal vasculature as shown in Fig. 1, in a cross-sectional image of the right kidney, suggesting significantly reduced renal perfusion and thus reduced depictable vasculature in a child with renal failure. **b** Reduced renal perfusion in a child with left renal hypodysplasia with diffusely reduced renal vasculature seen as renal vessel rarefaction on ACDS. Note the vascularity of the adjacent spleen for comparison

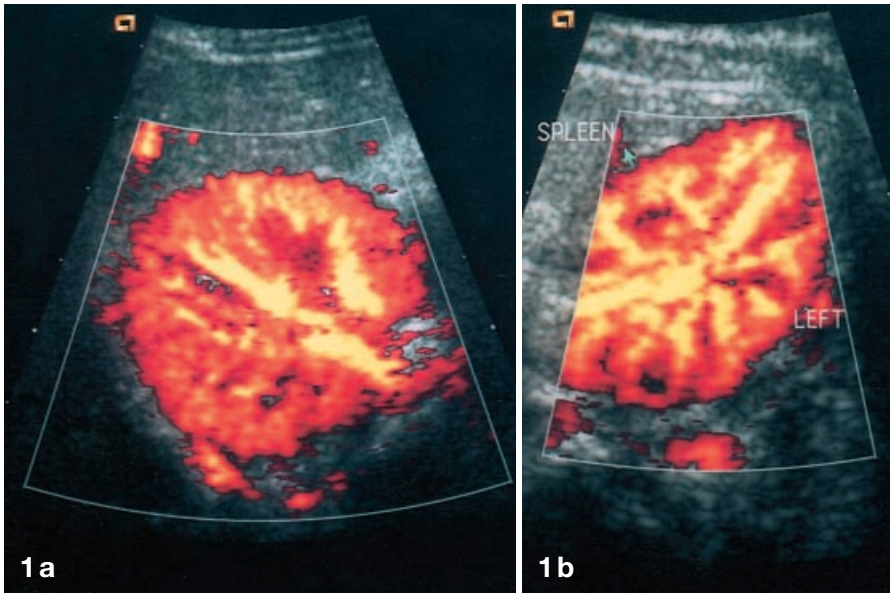
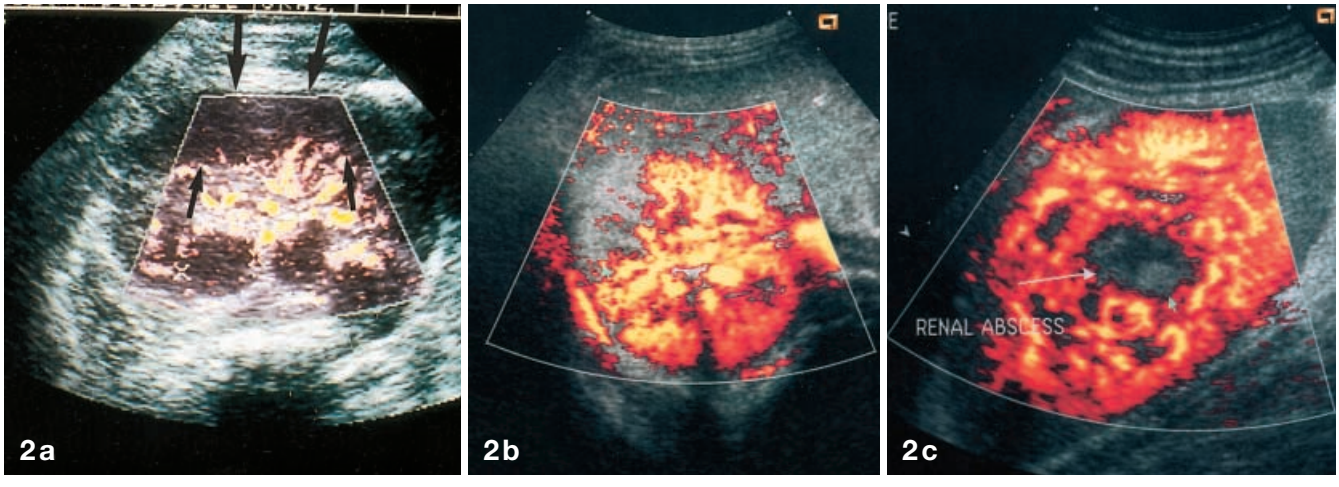


Fig. 1a, b Amplitude CDS of a healthy kidney: demonstration of normally perfused renal vasculature including cortical vessels on this cross-sectional image, with physiologically hypovascular medulla compared with the cortex. **a** Right kidney of a child; **b** left kidney in a of non-sedated infant (9 months old)



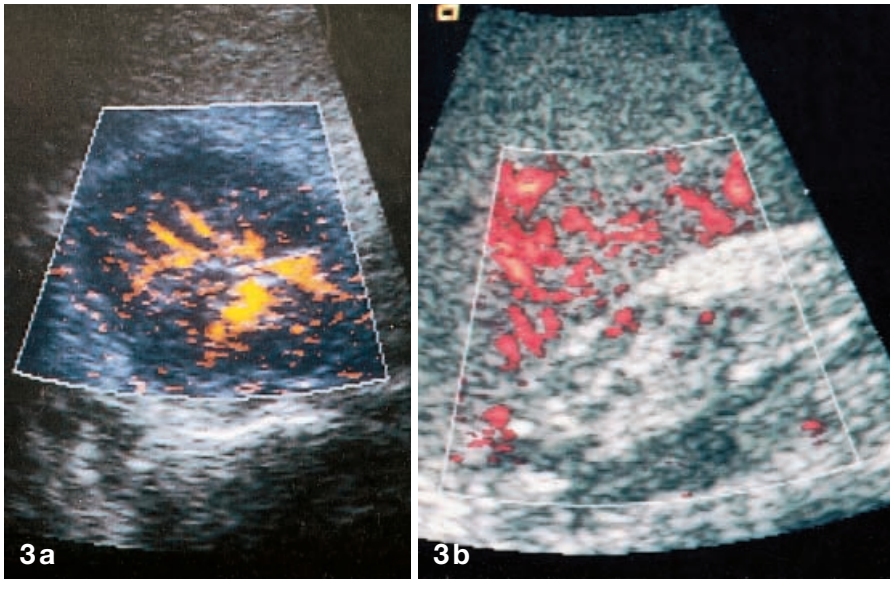


Fig. 2a–c Amplitude CDS of a focal perfusion defect. **a** Demonstration of well-defined hypoechoic areas without cortical and peripheral renal perfused vasculature *(arrow)* in a child with lymphoma, thus suggesting renal involvement and infiltration, as confirmed by contrast-enhanced spiral CT and on follow-up during and after treatment. Note generally reduced display of vessels also in the central parts. **b** Transverse view of the right kidney: ACDS demonstrates a segmental perfusional defect in segmental pyelonephritis. **c** ACDS demonstrates an area without perfusion/vasculature in this longitudinal section of the right kidney, representing a renal abscess *(arrow)*

Table 1 Patient data and results

Diagnosis	Total number	Inadequate exam	ACDS wrong / in number of reliable exams	ACDS correct (% of adequate exams)	Scinti-graphy	CT
Group 0	54	3	2 of 51	49 (96.1)	48	6
Group 1	43	4	4 of 39	35 (89.7)	33	6
Group 2	83	10	15 of 73	58 (79.5)	63	2
Total	180	17	21 of 163	142 (87.1)	144	14

ACDS results of healthy kidneys, kidneys with focally or diffusely impaired renal vasculature/perfusion and the individual number of scintigraphic and CT examinations categorised according to the final diagnosis (as shown by other modalities or clinical and laboratory as well as histology results). Group 0 = healthy kidneys; group 1 = focal lesions; group 2 = diffuse renal involvement

patients presented bilateral disease such as systemic LE, various forms of nephritis, bilateral reflux or bilateral urinary tract malformation, acute renal failure, haemolytic uraemic syndrome, infiltration in systemic lymphoma and bilateral nephroblastomatosis with unilateral Wilm's tumour.

In group 0, ACDS was successful in 51 of 54 healthy kidneys. In three infants the investigation failed due to motion and/or overlying bowel gas, causing either flash artefacts or forcing the investigator to decrease gain and sensitivity for scanning the kidney (especially the left kidney). Kidneys with compensatory hypertrophy were included in this group, because this was considered a healthy, normal state provided scintigraphy had proven these kidneys to be otherwise normal. Scintigraphy was available in 48 kidneys; 6 kidneys had undergone CT. Amplitude CDS demonstrated unimpaired renal vasculature in 49 of the 51 healthy kidneys (Fig. 1). Accuracy was 96.1 % in the 51 patients with satisfactory ACDS exams (Table 1). The two false results were normal kidneys showing regionally decreased perfusion on ACDS, probably due to a mix of artefacts caused by gain manipulation, penetration issues (rip shadowing, different depth of upper and lower pole), and adjacent bowel gas causing higher filter settings leading to less signal at poor angles (upper/lower pole).

Forty-three kidneys of group 1 suffered from purely focal disease such as focal pyelonephritis, cystic lesion, tumour or focal infiltration, as well as scars (as shown by scintigraphy, CT, IVP and MRI) or focally diminished perfusion after renal biopsy. Scintigraphy was available in 33 kidneys; 6 kidneys had undergone CT. Amplitude CDS could be adequately performed in 39 kidneys and correctly depicted focal lesions in 35 kidneys with a percentage of agreement of 89.7 % (Fig. 2; Table 1). Again, the cause for inadequate ACDS investigations was motion and/or overlying bowel. Most of the scars were picked up by grey-scale imaging; however, ACDS depicted an additional five scars in five kidneys with diffusely increased echogenicity, and six additional focal lesions were more readily depicted by ACDS, thus yielding a higher diagnostic confidence.

Eighty-three kidneys of group 2 had diffuse involvement secondary to renal failure, involvement in systemic disease, RNP, and diffuse inflammation (as shown on scintigraphy and/or laboratory proof for renal involvement in urinary tract infection), or glomerulonephritis and nephrotic syndrome; some of them also had additional focal lesions on scintigraphy. These additional focal lesions were not included in this study, and, even in retrospect, were hard to identify on ACDS. The contralateral kidneys with compensatory hypertrophy in unilateral diffuse disease (e. g. such as diffuse involvement in urinary tract infection, obstructive/refluxive hypodysplasia, atrophy) were included in group 1, as compensatory hypertrophy was considered a normal, "healthy" status. Scintigraphy was available in 63 kidneys; 2 kidneys had undergone CT. In 73 kidneys (88 %) ACDS investigations of diagnostic quality could be obtained; ACDS depicted diffuse reduction in vasculature/perfusion in 58 patients (69.9 % of the total number) with a percentage of agreement of 79.4 % (Fig. 3; Table 1). In 8 of the false-negative cases, differentiation between unsuccessful imaging, due to motion and artefacts, and therefore the need to change the ACDS settings (e. g. decreasing sensitivity or gain and increasing filter), and diffuse rarefaction of vessels or diminished perfusion was unreliable. Five of them again involved the left kidney; all were labelled as "without proof for disturbed perfusion". Diffuse hyperaemia in diffuse inflammation could not be appreciated due to missing possibility for quantification. No focal hyperaemia was observed, except for areas with relatively normal perfusion ("pseudohyperaemia") in inhomogeneous manifestation of renal damage.

In total, ACDS was applicable in 163 kidneys (90.6 %). Amplitude CDS was correct in demonstrating normal or impaired perfusion/vasculature in 142 kidneys (78.9 % of the total number), thus showing an overall percentage of agreement of 87.1 % in relation to the number of successfully performed investigations (Table 1). Despite additional information obtained by ACDS, the clinical impact in terms of a change in management was low. Amplitude CDS affected clinical management only in 10 patients, e. g. by demonstrating

focal infection (intravenous antibiotic treatment), reduced perfusion (vs nor perfusion) in renal failure (diuretic medication or need for haemodialysis), depicting renal involvement in LE (therefore renal biopsy was performed) and depicting areas of nephroblastomatosis; otherwise, clinical and laboratory data provided sufficient information to guide treatment and further management.

Discussion

Colour Doppler sonography is based on the mean frequency shift and is therefore subject to several limitations. It is angle dependent and the character of the background noise reduces its ability to depict peripheral vessels or space blood flow [8, 11, 12]. Due to its limitations, some areas remain inaccessible for CDS evaluation. High expectations arose with the advent of ACDS because the new method showed promise of being a superior tool for depicting perfusion and alterations of vasculature. The signal displayed in ACDS, i.e. the total integrated Doppler spectrum, is a complex function of the number of moving blood cells [1, 2, 6, 7]. Amplitude CDS is relatively independent of the insonation angle, thus becoming much more sensitive in depicting even low flow in vessels almost perpendicular to the US beam. Amplitude CDS sums up the venous and arterial Doppler activities, but this does not reduce its accuracy or sensitivity in showing flow and perfusion, and additional CDS and duplex evaluation can easily be performed when needed.

To date, only a few reports exist on the use of ACDS in children and infants [13, 14, 15, 16, 17, 18, 19, 20]. Although ACDS is able to demonstrate focally altered perfusion and improves assessment of diffusely altered renal perfusion, it relies on stringent operating conditions such as sufficient cooperation and the ability of the child to remain relatively still, as well as appropriate instrument settings [21]; thus, in some children (e.g. due to motion or increased breathing rate), the results of ACDS are inconclusive. However, in our experience, ACDS is applicable to the majority of patients including newborns and infants (Fig. 1; Table 1). The advantages of CDS are that it is less motion dependent and provides a quick differentiation of flow direction; therefore, CDS and ACDS are complementary methods. The applications depend on the clinical query. The combination of various US modes allow reliable analysis of renal perfusion and vasculature by a non-invasive and non-ionizing method that can be performed at the bedside on demand as often as necessary with relatively low costs. This promises to enlarge the field of renal US applications, with an acceptable sensitivity and specificity, close to those offered by other imaging methods such as CT and MRI, at least with regard to achieving fast first diagnostic information or for follow-up studies. Further technical development of this technique (e.g. fewer artefacts, faster frame rates, quicker switching times, introduction of echo-enhancing materials, enabling also dynamic perfusion studies, three-dimensional ultrasound) will probably expand the paediatric applicability.

Problems arise with diffusely impaired perfusion, because no proper gold standard for gain setting is present and quantification is impossible. Comparison to the vasculature of the spleen is helpful but still remains not as valuable as the comparison with the healthy contralateral kidney, which can only be applied to patients with unilateral disease. Due to the lack of a general baseline standard, ACDS performs poorly in demonstrating increased perfusion as particularly observed in arteriovenous fistulas after renal biopsy [22]; however, ACDS appears to be a good tool for depicting diminished perfusion. Amplitude CDS has been shown to be helpful in evaluating renal response in equivocal UPJO showing diffuse peripheral vessel rarefaction/cortical deterioration of perfusion after administration of furosemide to provoke acute obstruction [23]. Furthermore, reports on differentiation of tubular necrosis vs acute renal ischaemia in transplanted kidneys document the possible benefit of ACDS in acute and diffuse renal disease [5]. No reports of prospective studies exist on ACDS application in acute renal failure and other systemic renal disease. In general, we believe that ACDS is necessary to depict disease such as focal infection, infarction and infiltration, or for differential diagnosis of acute tubular necrosis vs vascular impairment. Amplitude CDS is useful for evaluating scarring, dysplasia, nephroblastomatosis, evaluation of renal perfusional impairment in renal failure or glomerulonephritis/nephrotic syndrome, and is probably useless for diagnosis of arteriovenous fistulas, in all situations where conventional US and CDS already were conclusive, or in disease without vascular/perfusional renal impairment.

Static DMSA scintigraphy does not directly show renal perfusion but demonstrates parenchymal function. However, since function often corresponds to perfusion, we consider scintigraphy to be a well-established modality and a reliable counterpart for evaluating ACDS. Considering our task to reduce irradiation in paediatric radiology, we decided not to perform CT in all study patients, but only when clinically indicated: the good correlation of ACDS with multiphasic contrast-enhanced CT has already been reported [15, 18].

In conclusion, the results suggest that ACDS is a reliable technique applicable to paediatric renal disease in the majority of paediatric patients. The results in this study correlate well with clinical, scintigraphic biopsy and CT findings. As long as the limitations of ACDS are recognised, ACDS will be a useful adjunct to conventional sonography, including CDS, and may provide, in the individual case, reliable diagnostic information.

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