Continuous renal replacement therapy: should the cardiologist be able to manage it out of intensive care units?

Continuous renal replacement therapy: Should the cardiologist be able to manage it out of intensive care units?

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Continuous renal replacement therapy (CRRT) has received increasing attention in recent years parallel to the publication of several favourable data regarding the use of this technique in different clinical conditions such as congestive heart failure (CHF) [1,2] and contrast induced nephropathy (CIN) [3,4]. Moreover, the improvement in technology has led to the diffusion of devices easier to use, that can be managed in Cardiology Units also out of the intensive care setting, overcoming logistic and practical problems.

CRRT can be performed in cardiac patients with three different main techniques:

a) Slow Continuous Ultrafiltration (SCUF): removes plasma water thank to a transmembrane pressure gradient (diffusion); solutes are passively removed accompanying the plasma water flow (convection);
b) Continuous Veno-Venous Hemofiltration (CVVHF): removes solutes by means of convection but fluid loss determined by ultrafiltration is compensated by a reinfusion solution;
c) Continuous Veno-Venous Hemo-Diafiltration (CVVHDF): removes liquids and solutes with the implementation of both dialysis and hemofiltration.

From January 2005 to December 2010 132 patients were consecutively treated with CRRT in the Cardiac Step Down Unit (CSDU) of the University of Florence, consisting of eight monitored beds with a nurse/patients ratio of 1:4. In the present letter we report our experience with CRRT and, in particular, in-hospital outcomes of patients submitted to this procedure and data regarding safety of CRRT in a non-intensive environment.

The main indications to CRRT in our population were: decompensated CHF in 63 patients (47.7%), prevention or treatment of CIN in 42 patients (31.8%) and acute kidney injury (AKI) for several causes in 27 critical cardiac patients (20.5%).

CHF patients were treated with CRRT if they showed at admission signs of fluid overload with peripheral edema >2+ and at least one of the following: 1) pulmonary rales or crackling; 2) dyspnea; 3) third heart sound; 4) jugular venous distension; 5) positive epato-jugular reflux; 6) maximal systolic arterial pulmonary pressure above 50 mm Hg at echocardiogram; 7) radiographic pleural effusion. A clinical score was used to objectivate the severity of clinical status of our patients assigning one point for each sign or symptom mentioned above (minimum value 2, maximum 8). CHF patients submitted to CRRT were those unresponsive to diuretic therapy despite the increased doses. They were divided in two subgroups: a) those with serum creatinine >3 mg/dl or glomerular filtration rate (GFR) MDRD <30 ml/min/m^2 were treated with CVVHDF; b) those with serum creatinine <3 mg/dl or GFR MDRD between 30 and 60 ml/min/m^2 treated with SCUF. Diuretic therapy was withdrawn during CRRT.

CIN was defined as an absolute increase in serum creatinine ≥0.5 mg/dl from baseline or as a relative increase ≥25% from baseline within 48–72 hours after contrast medium administration after the

Table 1
Clinical and biohumoral parameters variations, modality of CRRT and its related complications in congestive heart failure patients.

Congestive heart failure patients, $n = 63$ (47.6%)			
Demographic features			
Age, years (mean ± SD)			71.6 ± 13.6
Male gender, *n* (%)			43 (68.2)
Hypertension, *n* (%)			33 (52.4)
Diabetes mellitus, *n* (%)			30 (47.5)
Dyslipidemia, *n* (%)			20 (15.1)
Chronic kidney injury, *n* (%)			37 (58.7)
Ischemic cardiomyopathy, *n* (%)			33 (25.0)
Primitive cardiomyopathy, *n* (%)			22 (16.7)
Valvulopathy, *n* (%)			8 (6.1)
Ejection fraction pre-CRRT (mean ± SD)			31.5 ± 14.9
In-hospital mortality, *n* (%)			8 (7.9)
Modality of CRRT			
SCUF, n (%)			33 (52.4)
CVVHDF, n (%)			30 (47.6)
Treatment length, hours [median (IR)]			48 (72–96)
Clinical and laboratory features	Admission (pre-CRRT)	Discharge (post-CRRT)	*p* Value
Serum creatinine, mg/dl (mean ± SD)	2.6 ± 1.5	2.6 ± 1.5	0.091
Clinical score [median (IR)]	5 (3.5 - 7)	1 (0–2.5)	<0.001
NT-proBNP [median (IR)]	16878 (8914–34015)	5114 (1648–12808)	<0.001
Patients in NYHA class I-II, *n* (%)	4 (6.3)	29 (46.0)	<0.001
Patients in NYHA classes III–IV, *n* (%)	59 (93.7)	34 (54.7)	<0.001
CRRT-related complications			
Anemia, *n* (%)		1 (0.8)	
Thrombocytopenia, n (%)		1 (0.8)	
Infection, *n* (%)		1 (0.8)	

SCUF, Slow Continuous Ultrafiltration; CVVHDF Continuous Veno-Venous Hemodiafiltration; CRRT, Continuous Renal ReplacementTherapy.

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Table 2
Clinical characteristics, complications and variation of creatininemia and urinary output in patients requiring CRRT for prevention or treatment of CIN and AKI.

Demographic features	Prevention of CIN, $n=22$ (16.7%)	Treatment of CIN, $n=20$ (15.2%)	Treatment of AKI, $n=27$ (20.5%)
Age, years (mean ± SD)	71.0 ± 12.4	77.0 ± 8.5	75.2 ± 10.5
Male gender, *n* (%)	16 (72.7)	14 (70.0)	14 (51.9)
Chronic kidney injury, *n* (%)	22 (100)	13 (65.0)	20 (74.1)
Diabetes mellitus, *n* (%)	9 (40.9)	9 (45.0)	14 (51.9)
Contrast medium volume, ml (mean ± SD)	275 (250–400)	300 (250–400)	n.a.
CRRT duration, hours [median (IR)]	32 (18–32)	36 (36–72)	42 (21–84)
In-hospital mortality	0	1 (5.0)	5 (18.5)
CRRT-related complications			
Anemia	1 (4.5)	1 (5.0)	1 (3.7)
Thrombocytopenia	0	0	1 (3.7)
Bleeding at the insertion site	0	1 (5.0)	0

Clinical and laboratory features									
	Adm.	Dis.	*P*	Adm.	Dis.	*P*	Adm.	Dis.	*P*
Serum creatinine mg/dl (mean ± SD)	2.8 ± 1.0	2.1 ± 1.0	<0.001	4.0 ± 1.5	2.6 ± 1.4	<0.001	4.5 ± 2.3	2.9 ± 1.9	<0.001
Urine output ml/kg/h (mean ± SD)	1.71 ± 0.39	2.30 ± 0.59	<0.001	0.39 ± 0.10	1.87 ± 0.61	<0.001	0.29 ± 0.12	1.22 ± 0.44	<0.001

CIN, contrast induced nephropathy; AKI, acute kidney injury; CRRT, Continuous Renal Replacement Therapy; Adm., admission; Dis., discharge.

exclusion of alternative causes. CIN prevention with CRRT was performed with CVVHF in patients with severe chronic renal dysfunction (GFR ≤30 ml/min/1.73 m^2) following Marenzi's protocol [3,4] and according to recent guidelines on myocardial revascularization [5]. Treatment of CIN with CRRT was performed with CVVHDF in patients with an increase in creatinine values ≥3 mg/dl associated with oliguria 48–72 hours after contrast medium administration.

AKI was defined as an increase in serum creatinine >0.3 mg/dl (≥24 μmol/l) or increase ≥150% (>1.5 fold) respect to baseline associated with a urine output <0.5 ml/kg/h for almost 6 hours [6]. In this group of patients treatment consisted in CVVHDF.

CRRT was usually performed with a double-lumen catheter placed in the femoral vein and connected to the PRISMA™ System (HOSPAL-GAMBRO DASCO, Medolla, Italy) or Aquadex Flex Flow S-100 (CHF Solutions, Inc., Brooklyn Park, MN 55428, USA) when only SCUF was indicated. Pre-dilution modality of treatment was preferred to post-dilution modality for its minor risk of filter clotting. Unfractioned heparin was used in all patients to prevent filter clotting maintaining aPTT between 40 and 60 s. In patients at high hemorrhagic risk aPTT was maintained under 40 s, optimizing blood flow and maintaining filtration fraction between 10% and 20%.

Anemia was defined according to TIMI minor bleeding classification and thrombocytopenia as a platelet reduction>50% respect to baseline.

Tables 1 and 2 show demographic and clinical characteristics of patients who underwent CRRT for CHF, CIN prevention/treatment or AKI, respectively, as well as variations in some parameters determined by CRRT.

CRRT was initially introduced in clinical practice in intensive care units for the treatment of AKI associated with critical conditions such as cardiogenic and septic shock. However, in the last few years the use of CRRT has been also extended to other conditions such as CHF and prevention or treatment of CIN, two conditions for which an intensive environment is not always required. Parallel to this, new technologies have become available offering devices that are easier to use, contributing to the diffusion of this treatment also out of the intensive care units.

These recent advances have led cardiologists to deal increasingly with this technique and nurses to be specifically trained to manage CRRT devices.

In agreement with this trend and with new evidences in this field, since 2005 we progressively introduced CRRT in our clinical practice; data reported in this letter suggest the safety and feasibility of this technique also in a CSDU.

In our CHF patients CRRT has been able to improve clinical status and determine a significant reduction in clinical score, NYHA class and pro-BNP plasma levels with low rate of complications. In our population CRRT was also used and resulted as effective in four patients in NYHA class II at variance with previous studies demonstrating its efficacy in patients with more advanced NYHA class [1,2].

Moreover, according to the studies by Marenzi et al. [3,4] and to recent guidelines on myocardial revascularization [5] we used CRRT also for CIN prevention in patients at high risk for this complication.

Our experience confirmed the efficacy of these techniques since no patient developed this complication and stable values of creatinine and higher urinary output after the procedure were observed.

Patients with AKI from other causes have been shown to benefit from CRRT even though they have, also in our population, a higher mortality, confirming data from the literature according to which renal dysfunction is one of the main determinant of in-hospital mortality [7–11].

In conclusion, our data suggest that cardiologists should be able to manage CRRT even out of an intensive care setting for almost these three subgroups of patients.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [12].

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Contrast transthoracic echocardiography versus transcranial Doppler for patent foramen ovale detection

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Contrast transthoracic echocardiography (c-TTE)[1,2] and contrast transcranial Doppler (c-TCD) [3,4] are widely used for noninvasive diagnosis of patent foramen ovale (PFO). We thought to evaluate in a large series of patients the concordance between c-TTE and c-TCD in right-to-left shunt (RLS) diagnosis and in quantification. From June 2006 to July 2009 RLS was looked for in two hundred thirty two consecutive patients (160 females, aged 42.6 ± 15.3 years) who underwent on succession c-TCD and c-TTE at echocardiography laboratories of San Paolo and Dell'Angelo Hospitals (Milano and Mestre-Venezia, Italy). All patients gave their informed consent. The reason for RLS search was migraine in 167 patients (72%), stroke in 23 patients (9.9%), TIA in 29 patients (12.5%) and other causes in 13 patients (5.6%). Contrast TTE and TCD tests were performed using an agitated saline solution mixed with air [4]. Given that the Valsalva maneuver (VM) increases the sensitivity of RLS detection all patients were trained in VM execution. In all cases the study begun with c-TCD. In case of no or little microbubbles (MB) detection at the MCA the test was repeated with VM. Results were classified in a four-level categorization according to MB appearance in the TCD spectrum as follows: 0 indicates no occurrence of MB (test negative), 1 indicates 1–10 MB (small shunt), 2 indicates >10 MB without "curtain" effect (medium shunt) and finally 3 indicates "curtain" effect, whereas MB are so numerous that a single MB cannot be discriminated within the Doppler spectrum (large shunt) [4]. Subsequently patients underwent c-TTE. Once again results were classified in a four-level categorization according to MB appearance in the left hear after complete opacification of the right atrium [2]: 0 indicates no occurrence of MB (test negative), 1 indicates <10 MB passed through the PFO (small shunt), 2 indicates a cloud of >10 MB documented in the left atrium (medium shunt) and 3 indicates opacification of the left heart (large shunt)[5]. Quantitative data were expressed as mean ± standard deviation. Inter observer agreement in the diagnosis and grading of RLS both on c-TCD and c-TTE was assessed by calculating the Kappa-statistic. Odds Ratios and 95% Confidence Intervals were calculated. The concordance between c-TCD and c-TTE scores was estimated using the Lin's concordance correlation coefficient and the Spearman's rho rank correlation coefficient. Finally, the optimal trade-off between sensitivity and specificity of c-TTE was estimated by means of Receiver Operating Characteristic (ROC) curve analysis. All calculations were repeated on split subgroups with homogeneous diagnostic question. Overall, we noticed an excellent interobserver agreement both in c-TCD RLS scoring (K = 0.962, 95%CI 0.93–0.99) and in c-TTE RLS scoring (K = 0.985, 95%CI 0.96–1.00). Subsequently, we compared the c-TCD and c-TTE RLS gradations. In the overall study population the concordance correlation coefficient (CCC) between c-TCD and c-TTE RLS scores was CCC = 0.68 (95%CI 0.60–0.74), indicating a moderate correlation between c-TTE and c-TCD. The Spearman's coefficient of rank correlation (rho) was 0.68 (95%CI 0.60–0.74) confirming a moderate correlation between the two diagnostic procedures. Correlation and concordance between c-TCD and c-TTE RLS gradations were then analyzed in two subgroups of patients with homogeneous diagnostic question. The CCC between c-TCD and c-TTE RLS scores was moderate in patients with migraine (CCC = 0.63, 95%CI 0.53–0.71), and was good in patients referred for cerebrovascular diseases (CVD) (CCC = 0.87, 95%CI 0.79–0.92). The Spearman's coefficient of rank correlation was 0.63 (95% CI 0.52 – 0.71) in patients with migraine and 0.88 (95%CI 0.80–0.93) in patients with CVD, confirming the good correlation between the two diagnostic procedures in this subgroup of patients. The diagnostic performance of c-TTE compared with the presence of MB on c-TCD is exhibited by the Receiver Operating Characteristic (ROC) curve (Fig. 1). RLS score ≥ 1 on c-TTE can predict the presence of MB on c-TCD with the highest trade-off between sensitivity and specificity both in CVD and in migraine. Nevertheless, in CVD patients c-TTE had a higher sensitivity (100.0; 95% CI 88.1–100.0) and specificity (73.9; 95% CI 51.6–89.8) than in patients with

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