I TRATTAMENTI EMODIALITICI CONTINUI (CRRT) IN UNITA' CORONARICA

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ASST Lecco

INDICAZIONI A CRRT

EXTRA-RENALI

SCOMPENSO CARDIACO
PROFILASSI CIN

TOSSICI DIALIZZABILI
RABDOMIOLISI
ACIDOSI LATTICA DA METFORMINA
SHOCK SETTICO

RENALI

AKI +
- *IPERKALIEMIA*
- *ACIDOSI*
- *SINDROME UREMICA*
- *SOVRACCARICO FLUIDI*

..refrattari

Kellum et al. Critical Care 2013, 17:204
http://ccforum.com/content/17/1/204

CRITICAL CARE

REVIEW

Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1)

John A Kellum*[1] and Norbert Lameire[2], for the KDIGO AKI Guideline Work Group[3]

AJRCM 2010;181:1128-55

American Thoracic Society Documents

An Official ATS/ERS/ESICM/SCCM/SRLF Statement: Prevention and Management of Acute Renal Failure in the ICU Patient

An International Consensus Conference in Intensive Care Medicine

Laurent Brochard, Fekri Abroug, Matthew Brenner, Alain F. Broccard, Robert L. Danner, Miquel Ferrer, Franco Laghi, Sheldon Magder, Laurent Papazian, Paolo Pelosi, and Kees H. Polderman, on behalf of the ATS/ERS/ESICM/SCCM/SRLF Ad Hoc Committee on Acute Renal Failure

AKI: Definizione

AKI	↑ serum creatinine level of ≥0.3 mg/dl	< 48 hours
	↑ serum creatinine level ≥1.5 times baseline	< 7 days
	Urine output <0.5 ml/kg/h	> 6 hours
AKD	Persistent AKI for	7-90 days
CKD	Persistent kidney disease for	>90 days

AKI: Stadiazione

Table 1

Classification/staging system for acute kidney injury

System	Class/stage	Serum creatinine criteria	Urine output criteria
RIFLE	Class R	Serum creatinine increase to 1.5-fold or GFR decrease >25% from baseline	<0.5 ml/kg/hour for 6 hours
	Class I	Serum creatinine increase to 2-fold or GFR decrease >50% from baseline	<0.5 ml/kg/hour for 12 hours
	Class F	Serum creatinine to 3-fold, GFR decrease >75% from baseline or serum creatinine ≥4 mg/dl (≥ 354 µmol/l) with an acute increase of at least 0.5 mg/dl (44 µmol/l)	Anuria for 12 hours
AKIN	Stage 1	Serum creatinine increase ≥0.3 mg/dl (≥26.4 µmol/l) or increase to 1.5-fold to 2-fold from baseline	<0.5 ml/kg per hour for 6 hours
	Stage 2	Serum creatinine increase >2-fold to 3-fold from baseline	
	Stage 3	Serum creatinine increase >3-fold from baseline or serum creatinine ≥4.0 mg/dl (≥354 µmol/l) with an acute increase o least 0.5 mg/dl (44 µmol/l)	
		Need for RRT	

KDIGO: AKI classification and criteria

Severity	Serum creatinine concentration	Urine excretion
1	1.5- to 1.9-fold within 7 d or ≥ 0.3 mg/dL within 48 h	<0.5 mL/kg/h over a period >6 h
2	2.0- to 2.9-fold	<0.5 mL/kg/h for >12 h
3	≥ 3-fold or serum creatinine ≥ 4 mg/dL with an acute increase ≥ 0.5 mg/dL	<0.3 mL/kg/h for >24 h or anuria >12 h

AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes

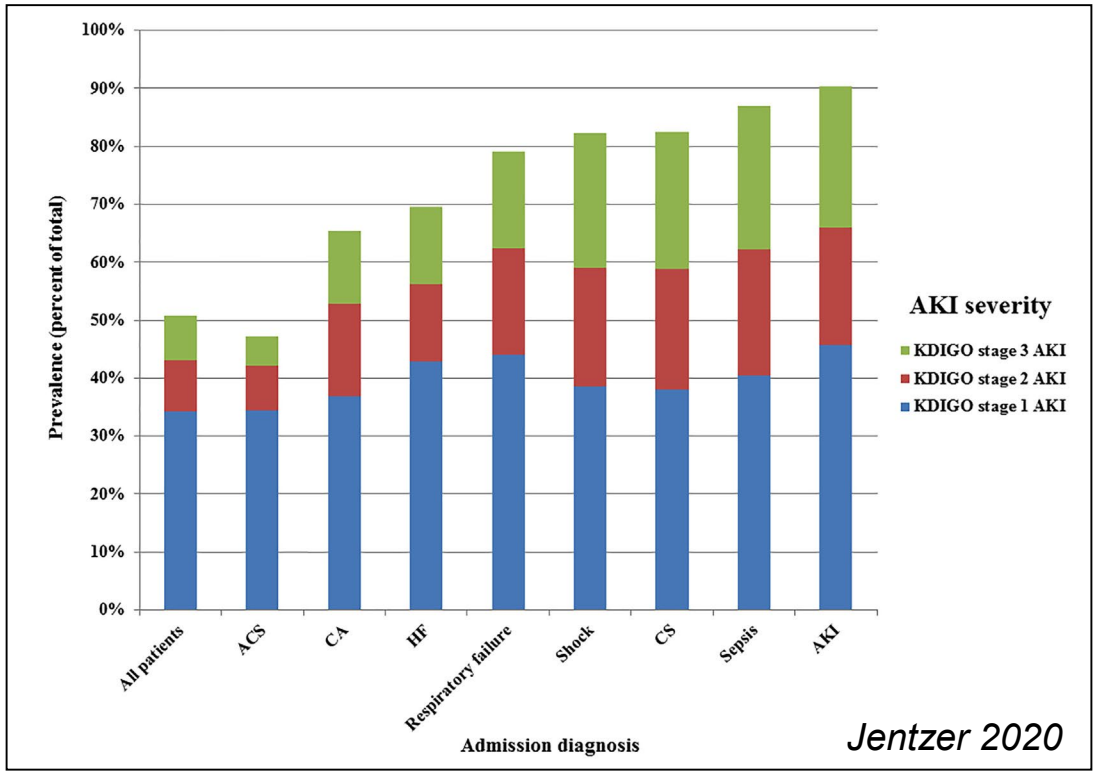
Epidemiologia dell'AKI in UTIC

Incidenza di AKI in pazienti ospedalizzati: 4-20%

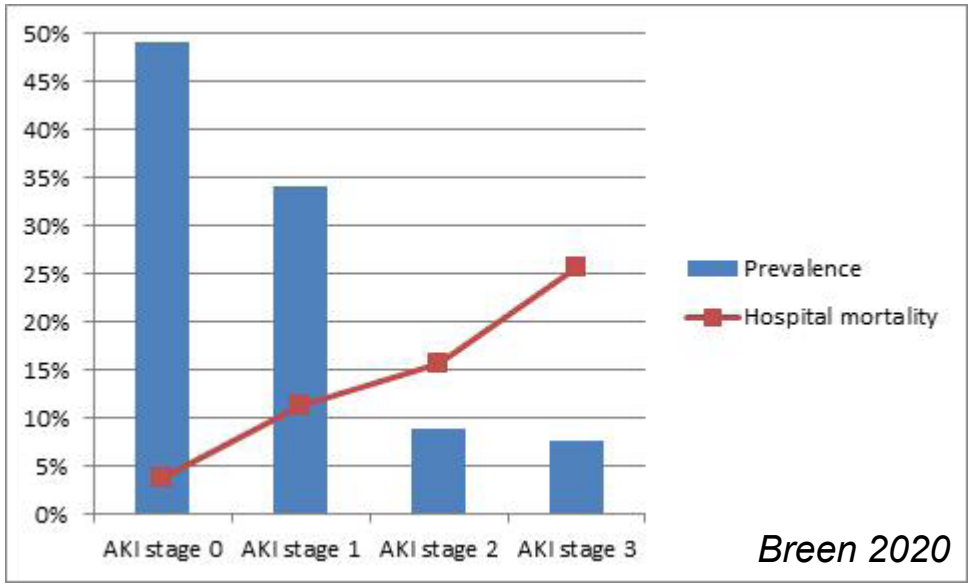
Incidenza di AKI in terapia intensiva: >60%

Incidenza di AKI in UTIC: 40-60%

Exposures	Susceptibilies
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female gender
Burns	Black race
Trauma	Chronic kidney disease
Cardiac surgery	Chronic diseases (heart, lung, liver)
Major noncardiac surgery	Diabetes mellitus
Nephrotoxic drugs	Cancer
Radiocontrast agents	Anemia



Jentzer 2020



Breen 2020

AKI: Eziologia

55-60%	PRE-RENALE	Shock – ADHF Ipovolemia	Ridotta PAM Aumento PVC
5%	POST-RENALE	Ostruzione vie escretrici (globo, idronefrosi)	Eco apparato urinario
35-40%	RENALE	- Necrosi tubulare acuta (mdc, sostanze tossiche, shock, sepsi) - Nefrite interstiziale (farmaci) - Glomerulonefrite - Vasculite - Occlusione acuta arteria/vena renale	Antibiotici, PPI Sedimento, ANA, ANCA, C3-C4 Doppler

European Heart Journal (2010) 31, 703–711
doi:10.1093/eurheartj/ehp507

Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative

Claudio Ronco[1,2]*, Peter McCullough[3], Stefan D. Anker[4,5], Inder Anand[6], Nadia Aspromonte[7], Sean M. Bagshaw[8], Rinaldo Bellomo[9], Tomas Berl[10], Ilona Bobek[1], Dinna N. Cruz[1,2], Luciano Daliento[11], Andrew Davenport[12], Mikko Haapio[13], Hans Hillege[14], Andrew A. House[15], Nevin Katz[16], Alan Maisel[17], Sunil Mankad[18], Pierluigi Zanco[19], Alexandre Mebazaa[20], Alberto Palazzuoli[21], Federico Ronco[11], Andrew Shaw[22], Geoff Sheinfeld[23], Sachin Soni[1,24], Giorgio Vescovo[25], Nereo Zamperetti[26], and Piotr Ponikowski[27] for the Acute Dialysis Quality Initiative (ADQI) consensus group

We considered definitions from the literature and used a specific publication[4] as template. We defined the broad term 'cardio-renal syndromes' as 'disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other'. We identified five subtypes of the syndromes (*Table 1*). Their pathophysiological mechanisms are described in *Figure 1*.

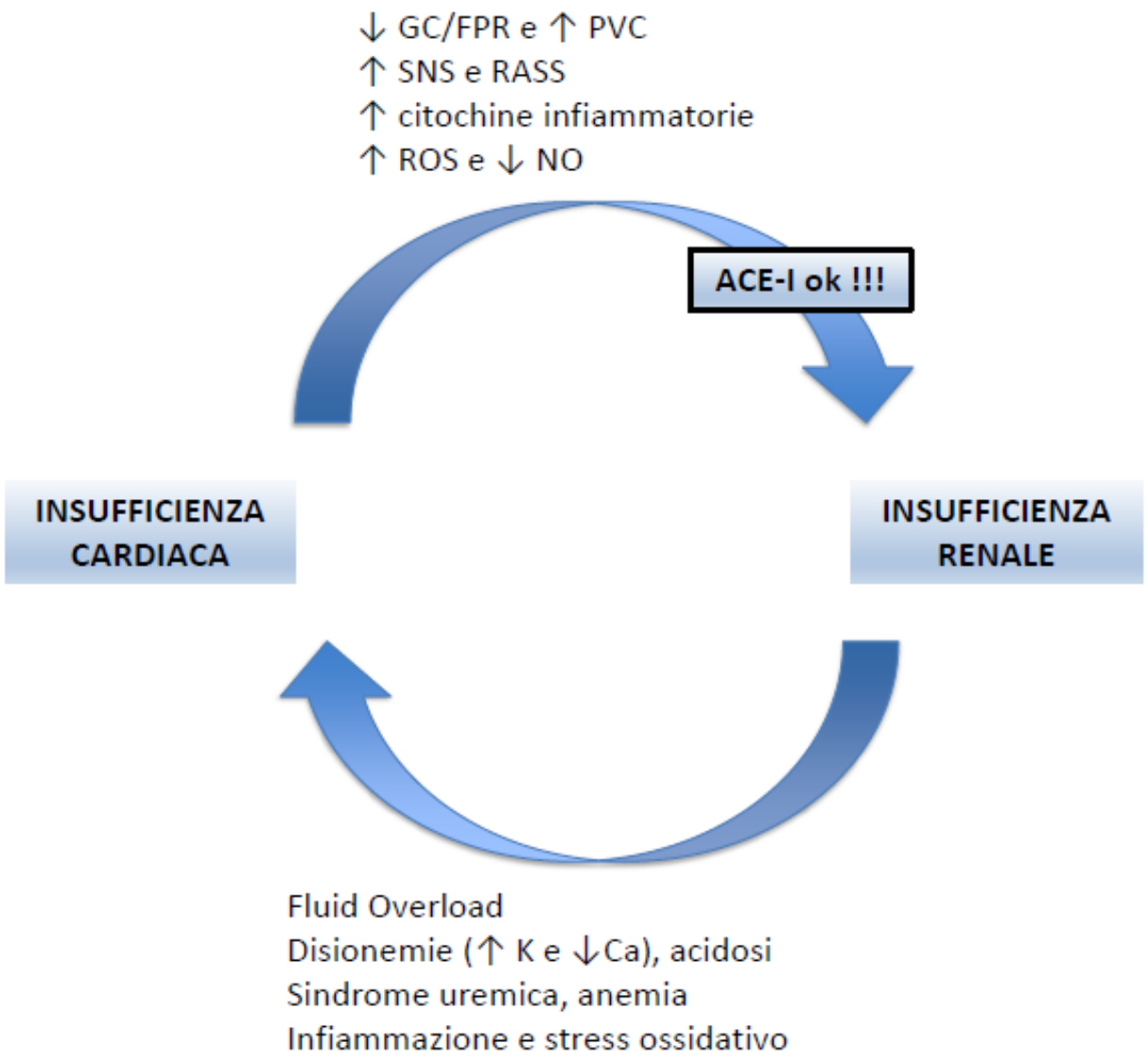
Table 1. Classification of CRS Based on the Consensus Conference of the Acute Dialysis Quality Initiative

Phenotype	Nomenclature	Description	Clinical Examples
Type 1 CRS	Acute CRS	HF resulting in AKI	ACS resulting in cardiogenic shock and AKI, AHF resulting in AKI
Type 2 CRS	Chronic CRS	Chronic HF resulting in CKD	Chronic HF
Type 3 CRS	Acute renocardiac syndrome	AKI resulting in AHF	HF in the setting of AKI from volume overload, inflammatory surge, and metabolic disturbances in uremia
Type 4 CRS	Chronic renocardiac syndrome	CKD resulting in chronic HF	LVH and HF from CKD-associated cardiomyopathy
Type 5 CRS	Secondary CRS	Systemic process resulting in HF and kidney failure	Amyloidosis, sepsis, cirrhosis

ACS indicates acute coronary syndrome; AHF, acute heart failure; AKI, acute kidney injury; CKD, chronic kidney disease; CRS, cardiorenal syndrome; HF, heart failure; and LVH, left ventricular hypertrophy.

CRS tipo 1:
25% dei pazienti ospedalizzati per ADHF (dei quali il 60% ha CKD)

CRS tipo 1: Patogenesi



CRS tipo 1: Patogenesi

Bassa portata e/o
Marcato aumento PVC/IAP

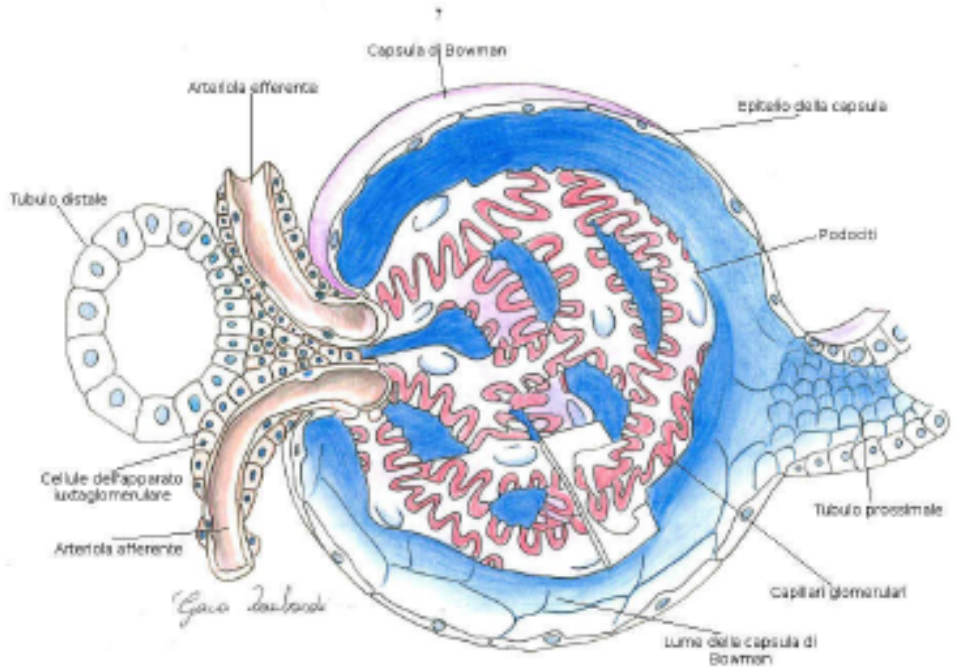
↓

Ridotta Pressione Perfusione Renale
(PPR = MAP – PVC/IAP)

↓

Ridotto Gradiente Filtrazione Renale
(GF = MAP – 2 IAP)

increased interstitial pressure with tubular collapse



Indicazioni all'avvio di CRRT

RENAL REPLACEMENT (indicazioni assolute)
A : metabolic **Acidosis** (pH <7.15)
E : **Electrolytes** (K >6.5 mEq/L or rapidly rising or ECG abnormalities)
I : **Ingestion** (certain alcohol or drug intoxications)
O: **Oliguria** with fluid **Overload** / diuretic-resistant pulmonary **Oedema**
U: **Uremia** (pericarditis, encephalitis, neuropathy, bleeding)

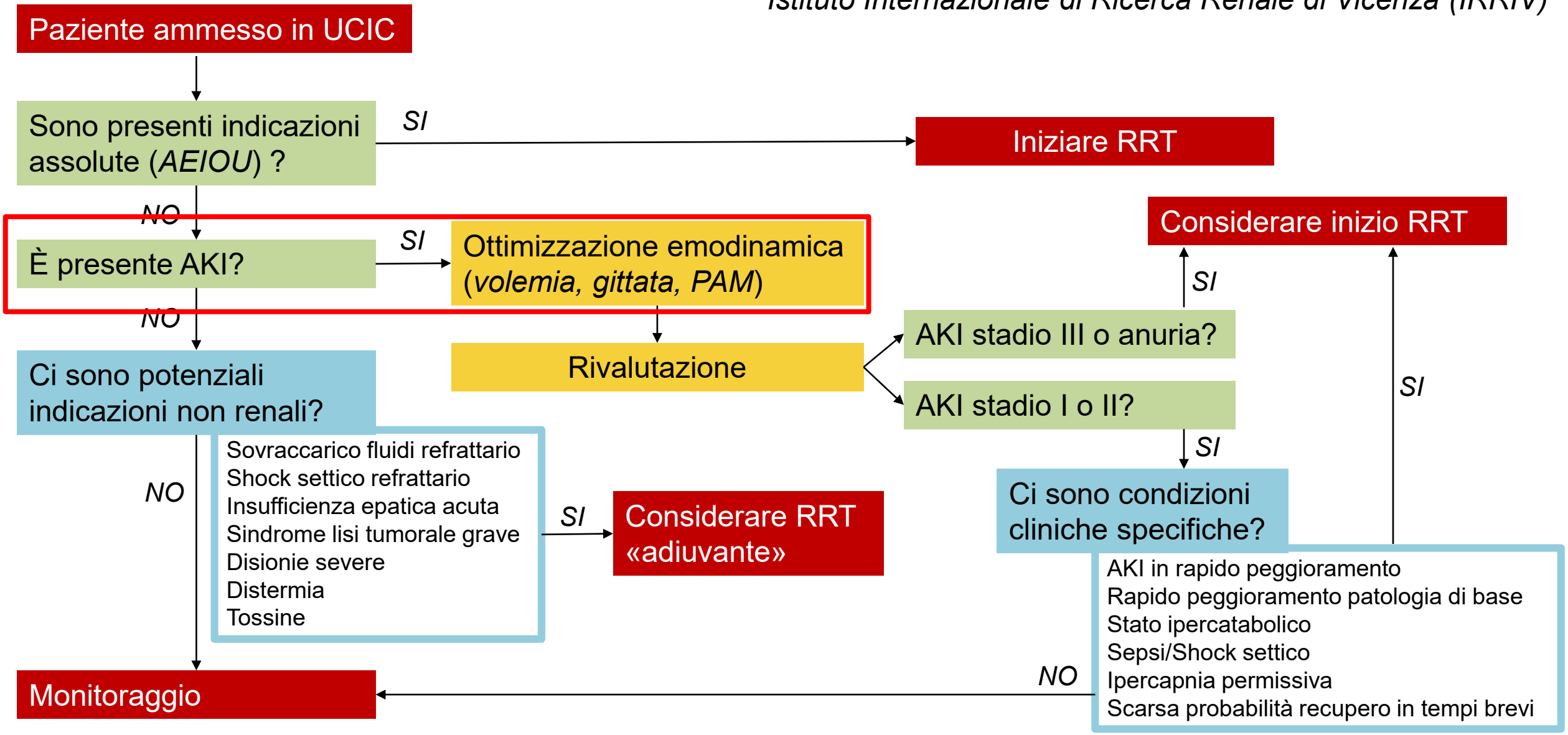
RENAL SUPPORT (prevenire è meglio che curare?)
Controllo dei soluti (creatinina,urea,citochine,lisi tumorale,mioglobina…)
Alterazioni dell'equilibrio acido-base e degli elettroliti
Controllo della volemia e del bilancio idrico

- Alta probabilità recupero renale
- Coagulopatia
- Carenza di accessi vascolari
- Scarsa tolleranza del paziente

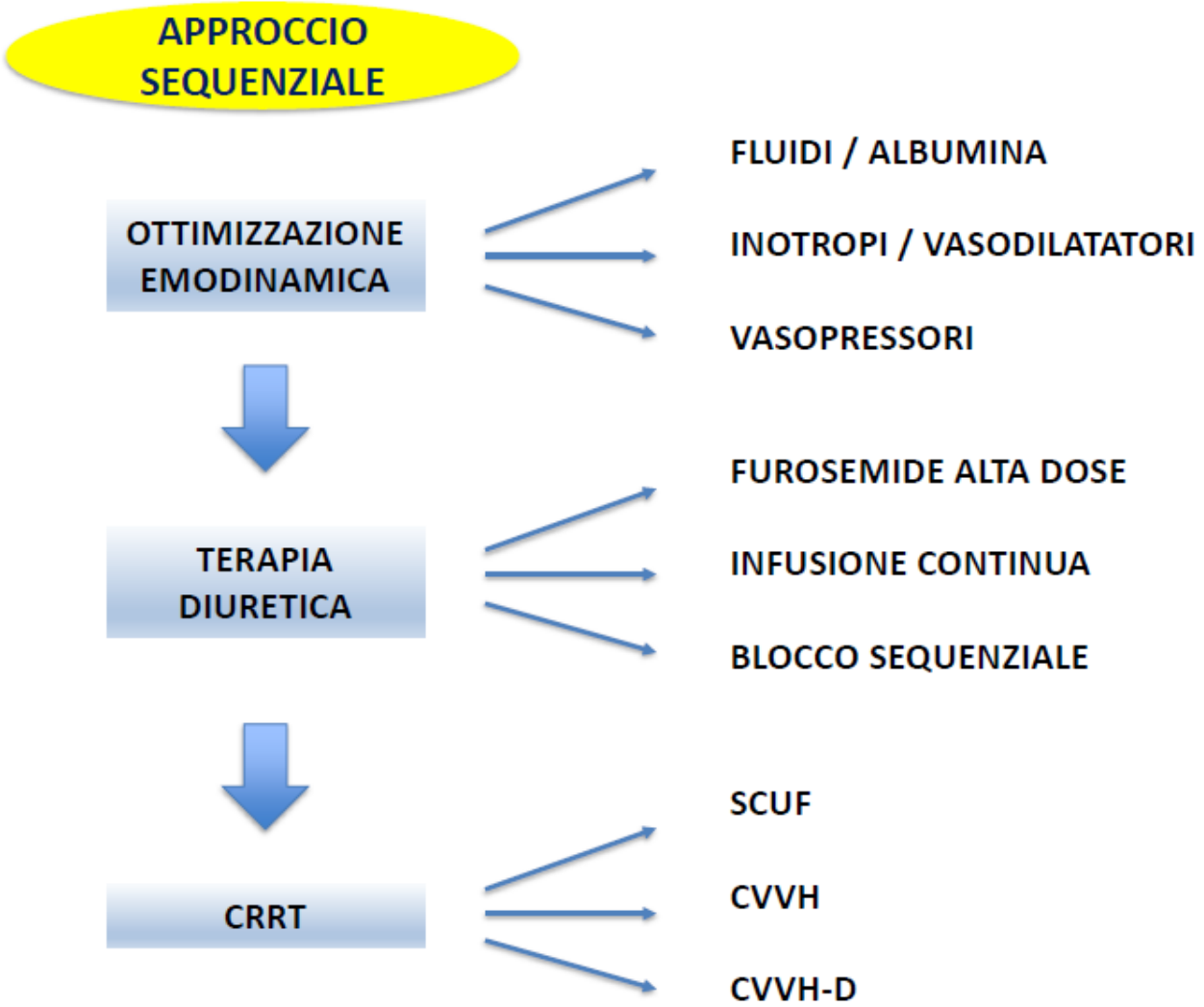
- Severità AKI
- Severità congestione
- Multi Organ Failure
- Iponatriemia
- Iperkaliemia
- Acidosi severa
- Iperazotemia severa
- Trend creatinina

Algoritmo decisionale

Istituto Internazionale di Ricerca Renale di Vicenza (IRRIV)



Algoritmo decisionale



(1) Escludere ipovolemia

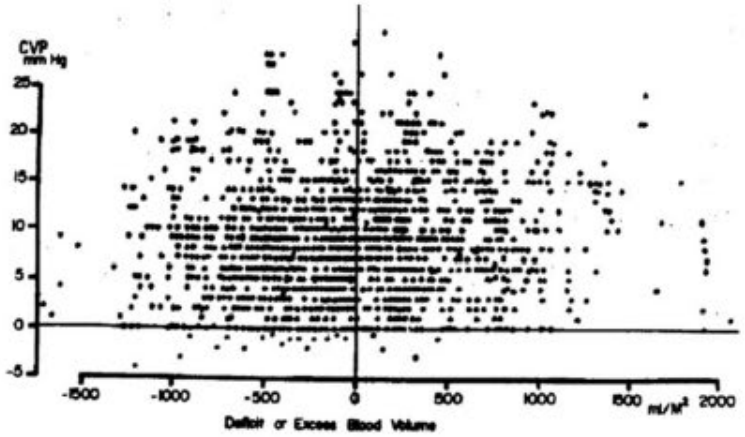
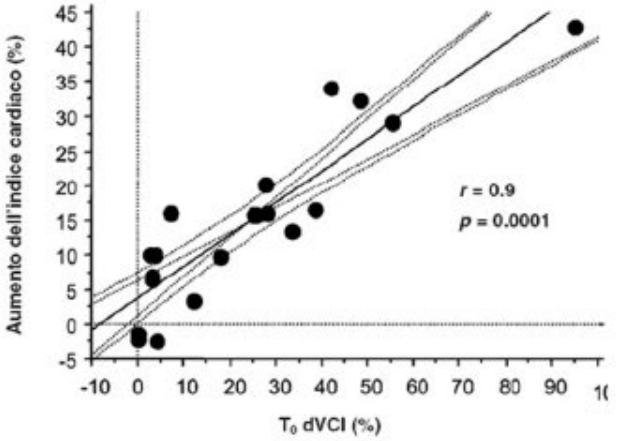
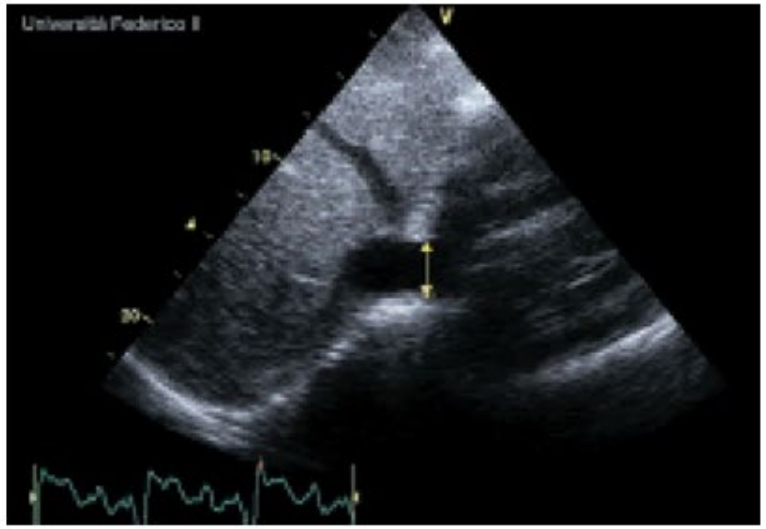
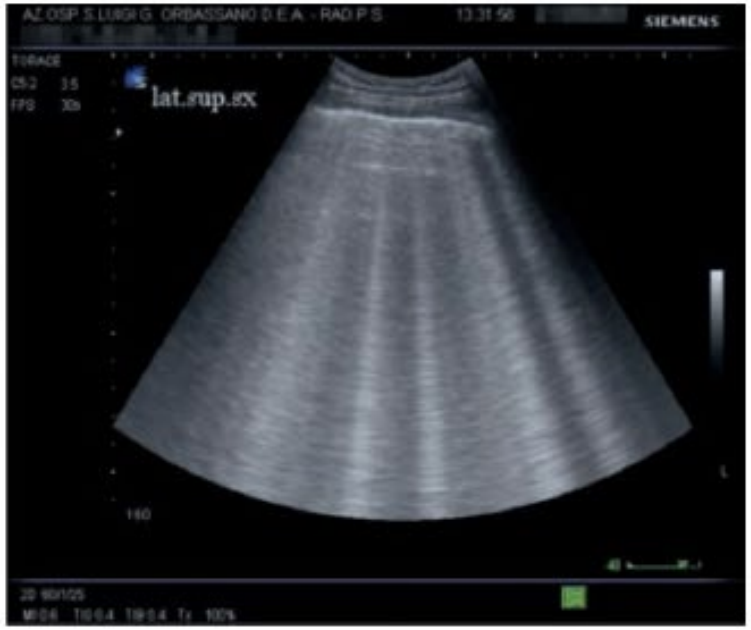


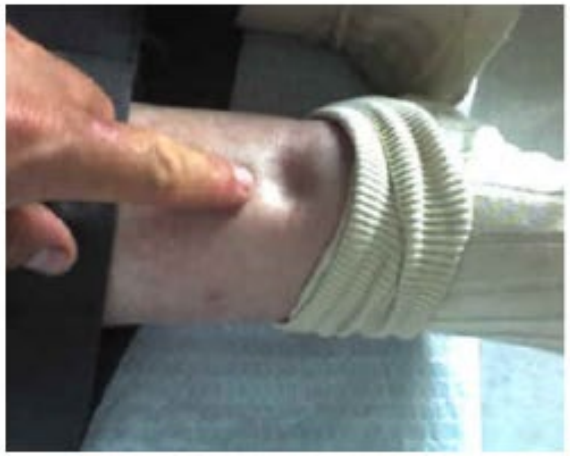
FIGURE 1. Fifteen hundred simultaneous measurements of blood volume and CVP in a heterogenous cohort of 188 ICU patients demonstrating no association between these two variables ($r = 0.27$). The correlation between ΔCVP and change in blood volume was 0.1 ($r^2 = 0.01$). This study demonstrates that patients with a low CVP may have volume overload and likewise patients with a high CVP may be volume depleted. Reproduced with permission from Shippy et al.[11]

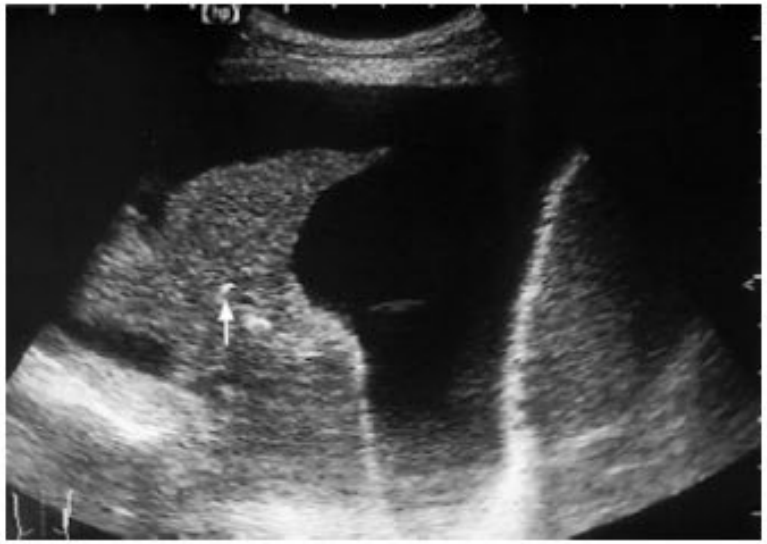




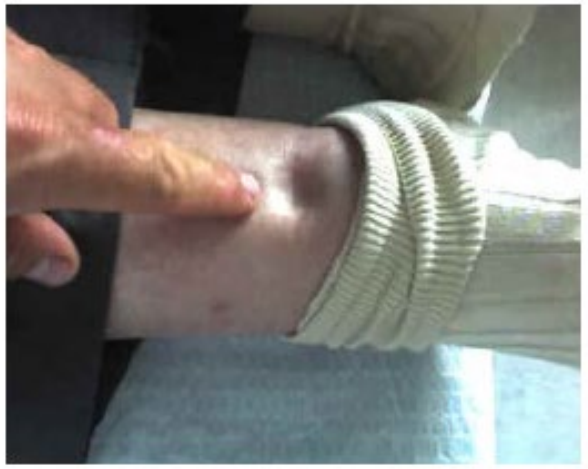
(2a) Presenza di Fluid Overload

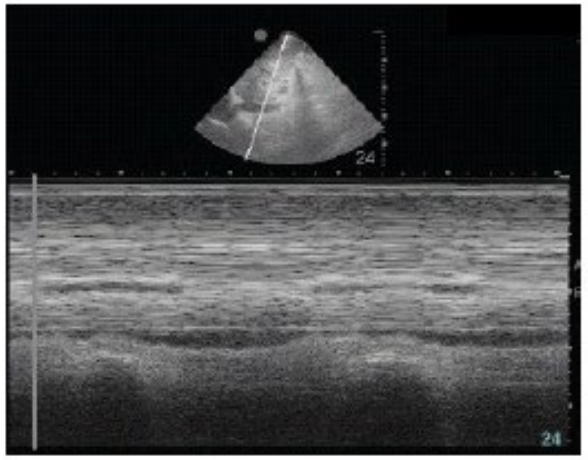






Pitfalls

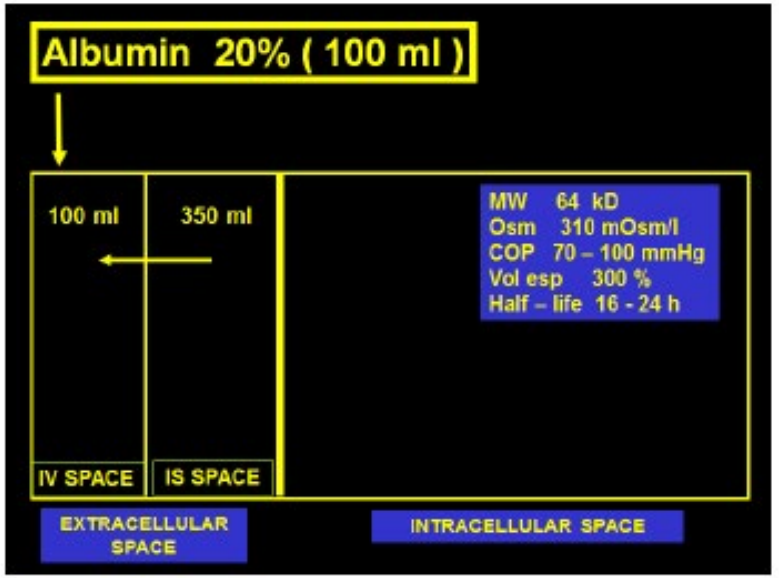




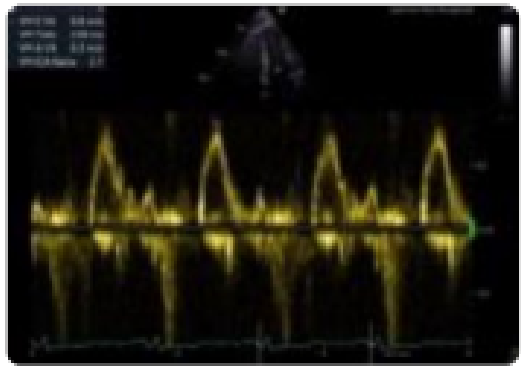
1) Scarico idrico lento (LASIX o SCUF)

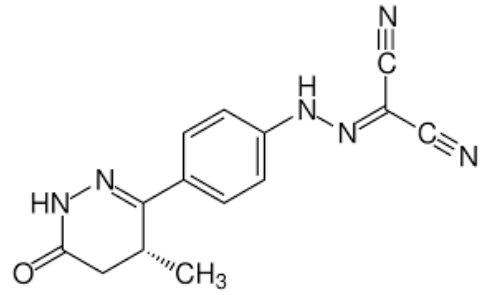
2) Monitoraggio (PA, FC, HCT)

3) Albumina ev



Do not fill when elevated (restrictive mitral inflow with E/A>1.8 and/or E/E'>15).





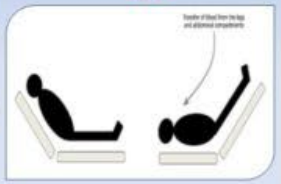
A restrictive mitral inflow may be observed in young patients (low LV compliance).
E/E' was mainly validated in cardiac patients.

EDITORIAL

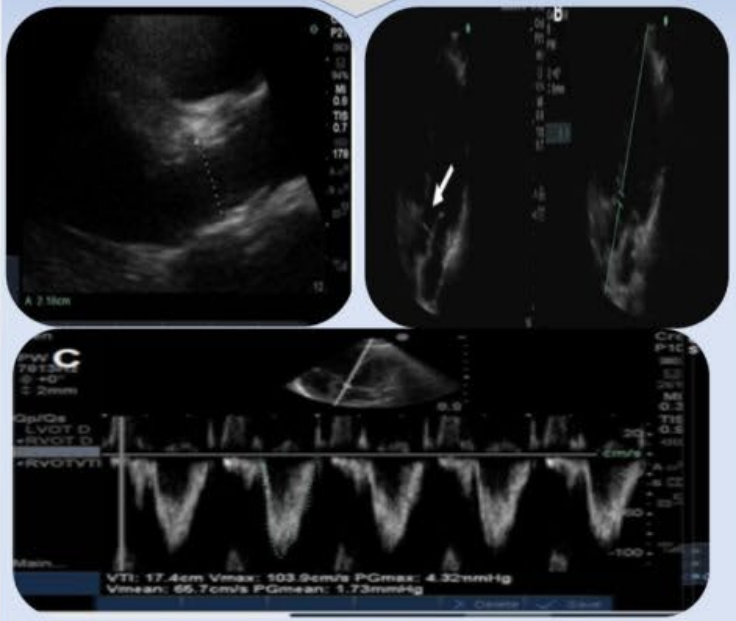
Using echocardiography to predict fluid-responsiveness and manage the need for fluids

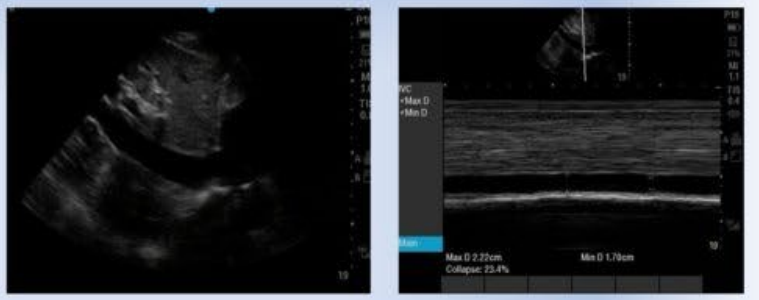
Antoine Vieillard-Baron[1,2*], Florence Boissier[3,4] and Michel Slama[5,6]

PoCUS Volume Assessment

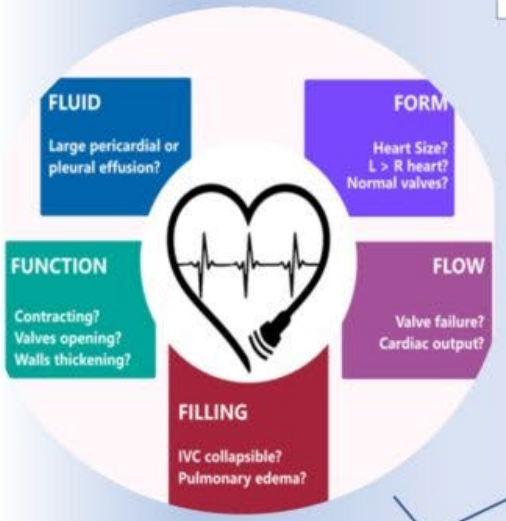


Assess Cardiac output Pre-Post PLR to determine fluid responsiveness





IVC size & CI

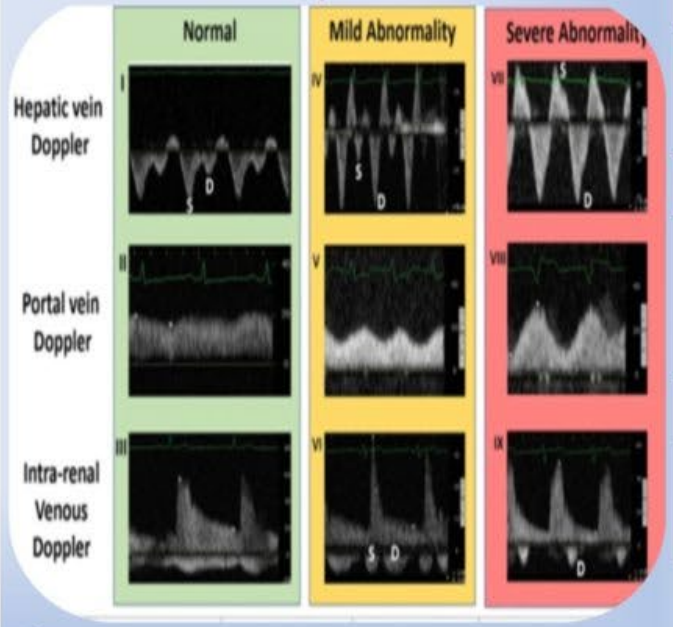


Focused cardiac ECHO to assess for effusion LV-RV function

Cardiac output (mL/min) = Stroke Volume (mL/cycle) x Heart Rate (bpm)
SV= LVOT area x LVOT VTI

Change > 10-15% suggest volume responsiveness

If IVC>2cm proceed for venous congestion assessment (VExUS)



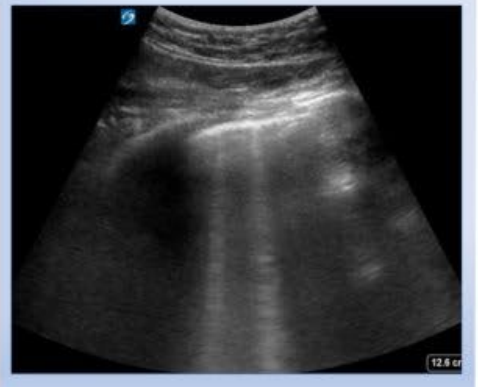
Grade 0
IVC<2cm

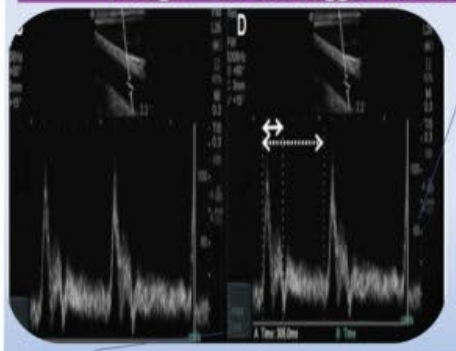
Grade 1
IVC>2cm
Veins NL or Mild

Grade 2
IVC>2cm
One severe vein

Grade 3
IVC>2cm
2 severe AbNL veins

B-lines and pleural effusion can represent interstitial lung syndrome and pulmonary edema





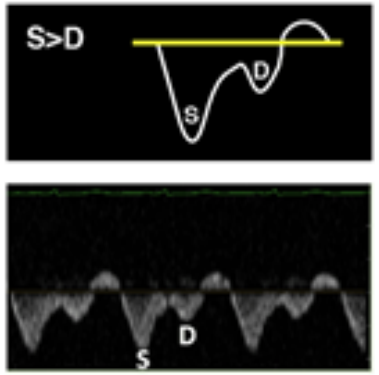
Carotid blood flow
$= \pi \times (\text{carotid diameter})^2/4$
× velocity time integral
× heart rate

Change >20% volume responsive

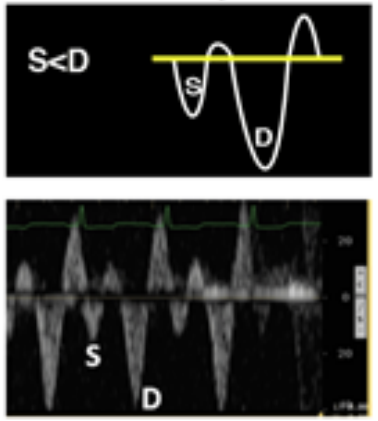
Corrected carotid flow time= systole time/√cycle time
Change > 15-25% suggest fluid responsive

References:
*Atkinson P, Peach M, Lewis D. Just the Facts: The Five F's of Focused Echocardiography in Shock. *CJEM*
Millington SJ, Wiskar K, Hobbs H, Koenig S. Risks and Benefits of Fluid Administration as Assessed by Ultrasound. Chest.
*Beaubien-Souligny W, Rola P, Haycock K, et al. Quantifying systemic congestion with Point-Of-Care ultrasound: development of the venous excess ultrasound grading system. *Ultrasound J.*

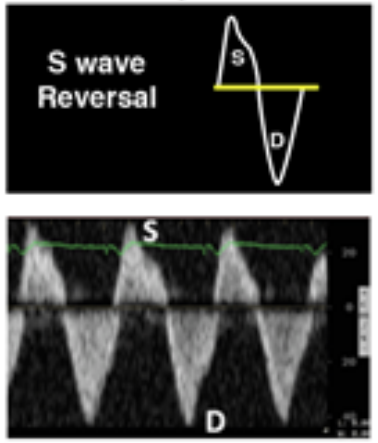
Normal Hepatic Vein Doppler: S>D



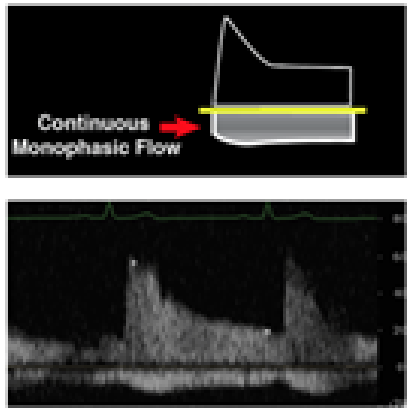
Mild Hepatic Vein Abnormality: S<D



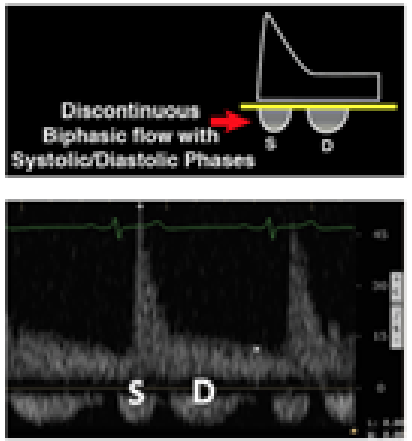
Severe Hepatic Vein Abnormality: S Reversal



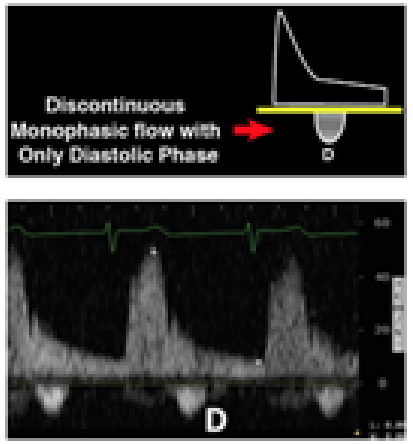
Normal Intrarenal Vein Doppler



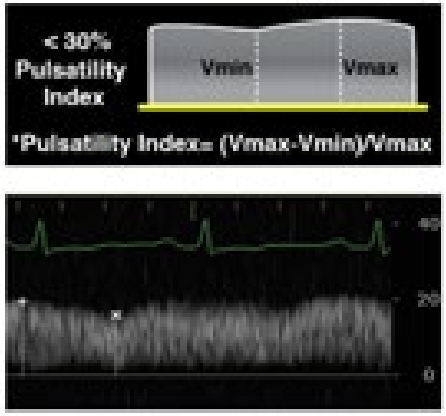
Mild Intrarenal Vein Abnormality



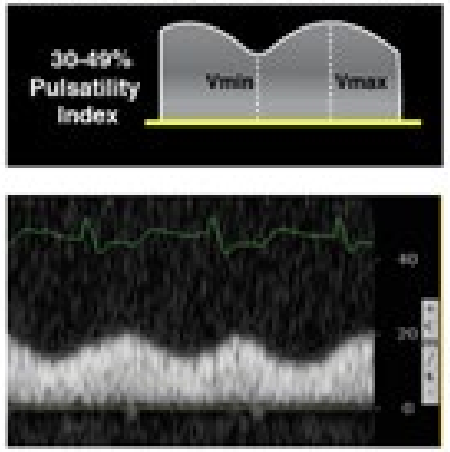
Severe Intrarenal Vein Abnormality



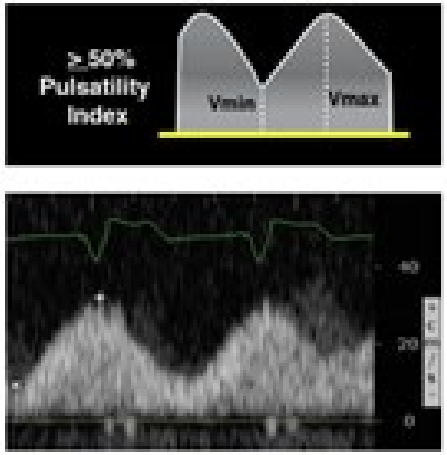
Normal Portal Vein Doppler



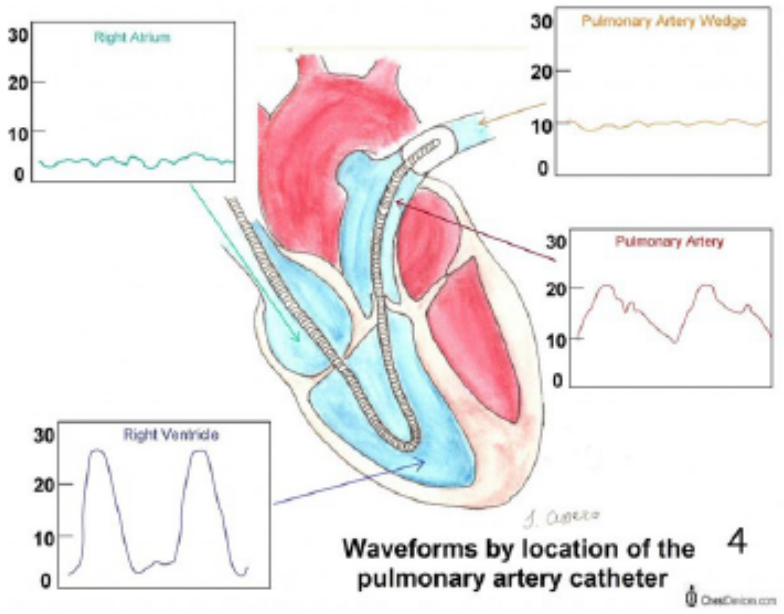
Mild Portal Vein Abnormality



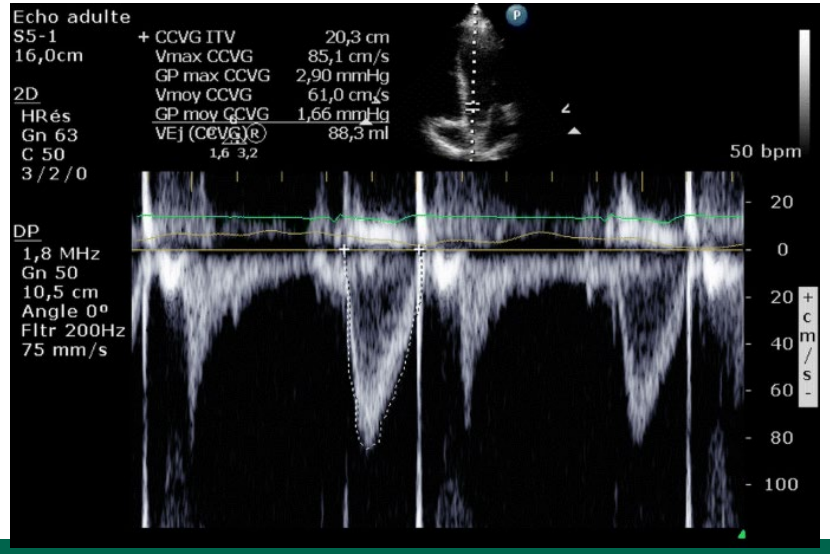
Severe Portal Vein Abnormality



(3) Ottimizzare portata cardiaca e pressione arteriosa



Waveforms by location of the pulmonary artery catheter 4

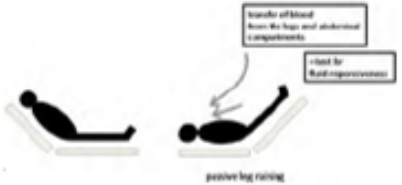


Valutare la FLUID RESPONSIVNESS…

Markers Statici
(PVC,WP;VTD)

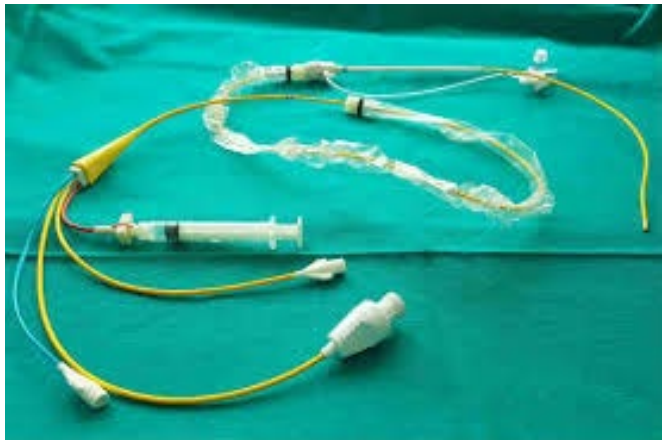
Indicatori dinamici
(PPV, SVV,CAVA)

INTERAZIONE CUORE-POLMONI

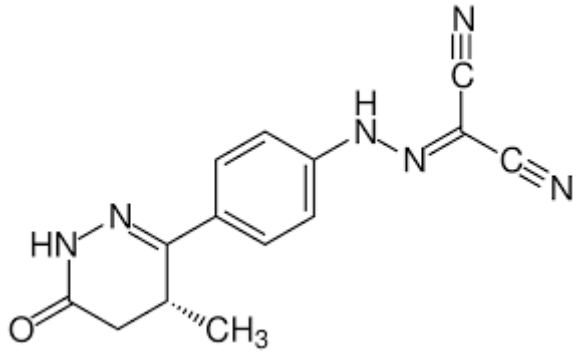


Nel paziente in respiro spontaneo o con aritmie

- LEG RAISING TEST
- FLUID CHALLENGE

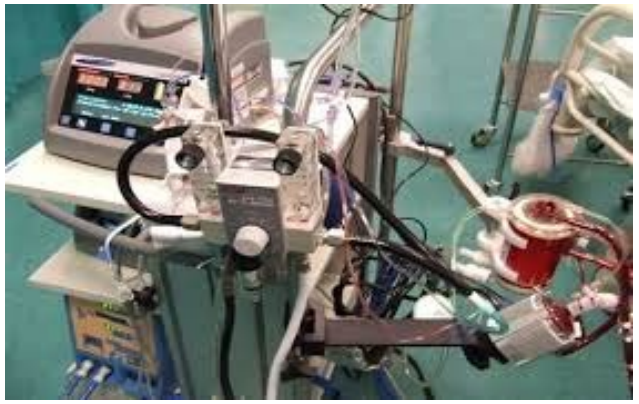


GC = (PAM - PVC) / SVR



Invasive Cardiac Hemodynamics

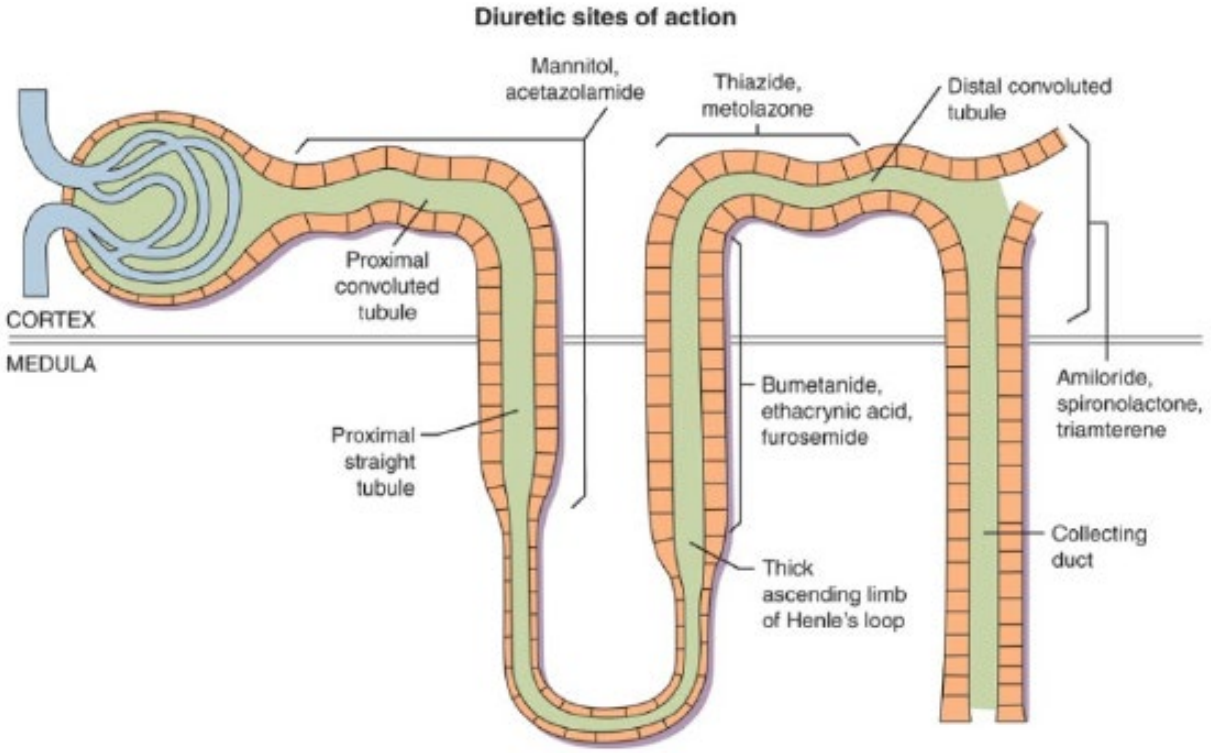
Metric	Calculation	Markers of cardiogenic shock
Cardiac index (CI)	CO/body surface area	≤2.2 L/min/m^2
Cardiac power output (CPO)	(MAP x CO)/451	<0.6 W
Cardiac power index (CPI)	(MAP x CI)/451	<0.4 W/m^2
Pulse pressure	systolic – diastolic blood pressure	<25 mmHg
Systemic vascular resistance (SVR)	[(MAP – CVP) / CO] x 80	variable
Right Ventricular Metrics	**Calculation**	**Markers of RV dysfunction**
Right atrial pressure (RAP)		>10/15 mmHg
Right atrial pressure (RAP) / Pulmonary capillary wedge pressure (PCWP)		>0.86 (in acute MI) >0.63 (after LVAD)
Pulmonary artery pulsatility index (PAPi)	(PASP-PADP) / RAP	≤0.9 (in acute MI) <1.85 (after LVAD)
Right ventricular stroke work index (RVSWI)	0.0136 x SVi x (mPAP–RAP)	<6 g/m/beat/m^2
Pulmonary Vascular Metrics	**Calculation**	**Markers of pulmonary vascular disease**
Transpulmonary pressure gradient (TPG)	mPAP-PCWP	≥12 mmHg
Diastolic pulmonary gradient (DPG)	PADP-PCWP	≥7 mmHg



(4) Trial di terapia diuretica

FUROSEMIDE IN INFUSIONE CONTINUA (max 2g/die) → **BLOCCO NEFRONICO SEQUENZIALE**

- Risparmiatore di potassio
- Acetazolamide
- Metolazone



Cause resistenza a furosemide:
- Ipoperfusione renale
- eGFR basso
- Ipoalbuminemia
- Acidi organici

ESC
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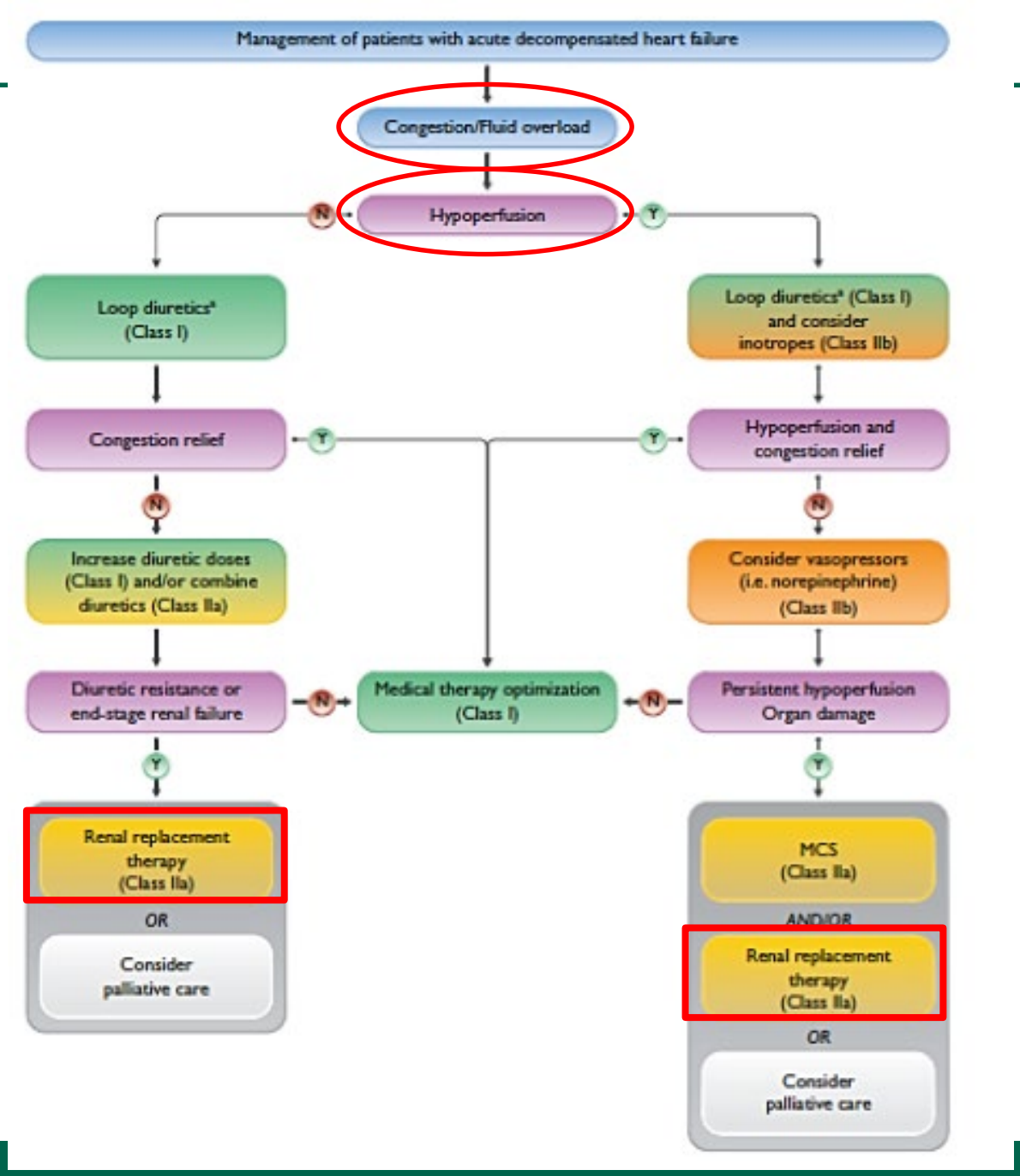
of Cardiology

2021



Quando iniziare la CRRT? Evidenze

Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury
The ELAIN Randomized Clinical Trial

ELAIN (2016)

INTERVENTIONS Early (within 8 hours of diagnosis of KDIGO stage 2; n = 112) or delayed (within 12 hours of stage 3 AKI or no initiation; n = 119) initiation of RRT.

RESULTS . Early initiation of RRT significantly reduced 90-day mortality (44 of 112 patients [39.3%]) compared with delayed initiation of RRT (65 of 119 patients [54.7%];

ORIGINAL ARTICLE

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

STARRT-AKI (2020)

METHODS

We conducted a multinational, randomized, controlled trial involving critically ill patients with severe acute kidney injury. Patients were randomly assigned to receive an accelerated strategy of renal-replacement therapy (in which therapy was initiated within 12 hours after the patient had met eligibility criteria) or a standard strategy (in which renal-replacement therapy was discouraged unless conventional indications developed or acute kidney injury persisted for >72 hours). The primary outcome was death from any cause at 90 days.

CONCLUSIONS

Among critically ill patients with acute kidney injury, an accelerated renal-replacement strategy was not associated with a lower risk of death at 90 days than a standard strategy. (Funded by the Canadian Institutes of Health Research and others; STARRT-AKI ClinicalTrials.gov number, NCT02568722.)

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

AKIKI (2016)

METHODS

In this multicenter randomized trial, we assigned patients with severe acute kidney injury (Kidney Disease: Improving Global Outcomes [KDIGO] classification, stage 3 [stages range from 1 to 3, with higher stages indicating more severe kidney injury]) who required mechanical ventilation, catecholamine infusion, or both and did not have a potentially life-threatening complication directly related to renal failure to either an early or a delayed strategy of renal-replacement therapy. With the early strategy, renal-replacement therapy was started immediately after randomization. With the delayed strategy, renal-replacement therapy was initiated if at least one of the following criteria was met: severe hyperkalemia, metabolic acidosis, pulmonary edema, blood urea nitrogen level higher than 112 mg per deciliter, or oliguria for more than 72 hours after randomization. The primary outcome was overall survival at day 60.

CONCLUSIONS

In a trial involving critically ill patients with severe acute kidney injury, we found no significant difference with regard to mortality between an early and a delayed strategy for the initiation of renal-replacement therapy. A delayed strategy averted the need for renal-replacement therapy in an appreciable number of patients. (Funded by the French

ORIGINAL ARTICLE

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

IDEAL-ICU (2018)

CONCLUSIONS

Among patients with septic shock who had severe acute kidney injury, there was no significant difference in overall mortality at 90 days between patients who were assigned to an early strategy for the initiation of renal-replacement therapy and those who were assigned to a delayed strategy. (Funded by the French Ministry of

Quale metodica scegliere?

METODICHE CONTINUE

1. Slow Continuous Ultrafiltration (SCUF)
2. Continuous Veno-venous Haemofiltration (CVVH)
3. Continuous Veno-venous Haemodyalisis (CVVHD)
4. Continuous Veno-venous Haemodyafiltration (CVVHDF)

Mantenimento stabilità emodinamica
Scelta trattamento in base a molecole da rimuovere
Miglior controllo ionico e acido-base

Paziente immobile
Complicanze catetere
Costi elevati

Indicate in:
- Pazienti emodinamicamente instabili (2B)
- Pazienti con traumi cerebrali acuti o altre cause di aumento pressione endocranica (2B)

METODICHE INTERMITTENTI

1. Intermittent Haeodyalisis (IHD)
2. Peritoneal dyalisis
3. Hybrid therapies

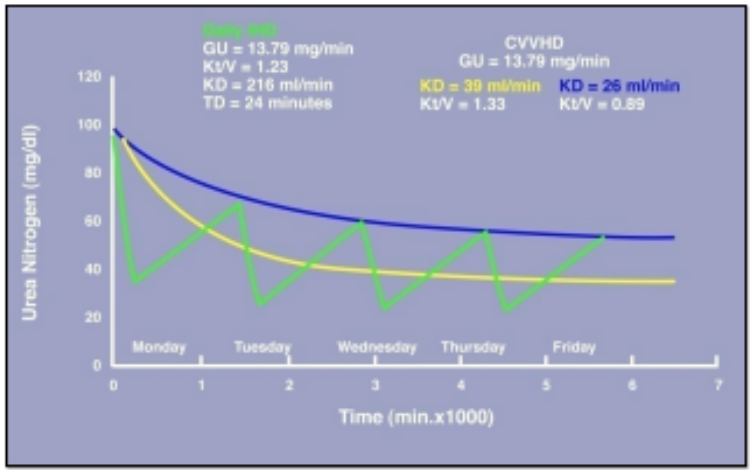
Possibile mobilizzazione
< complicanze infettive ed emorragiche
Costi minori (circa 50%)

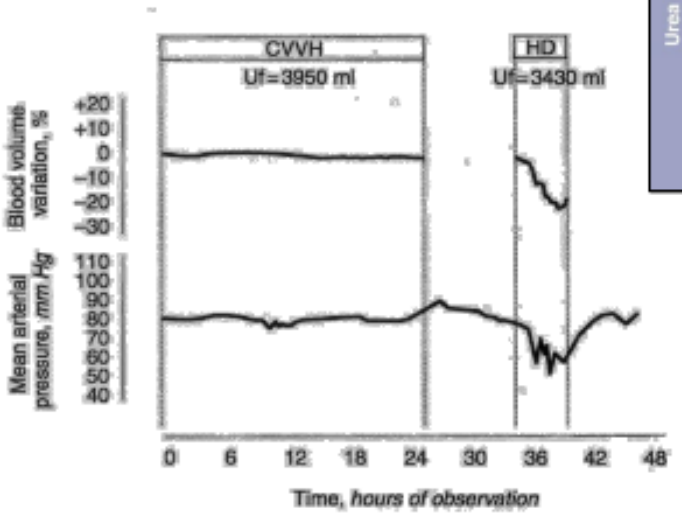
Instabilizzazione emodinamica
Fluttuazioni repentine P endocranica

Nessuna differenza in termini di mortalità

IHD = Qd 500-800 ml/min

CVVHD = Qd 15-50 ml/min



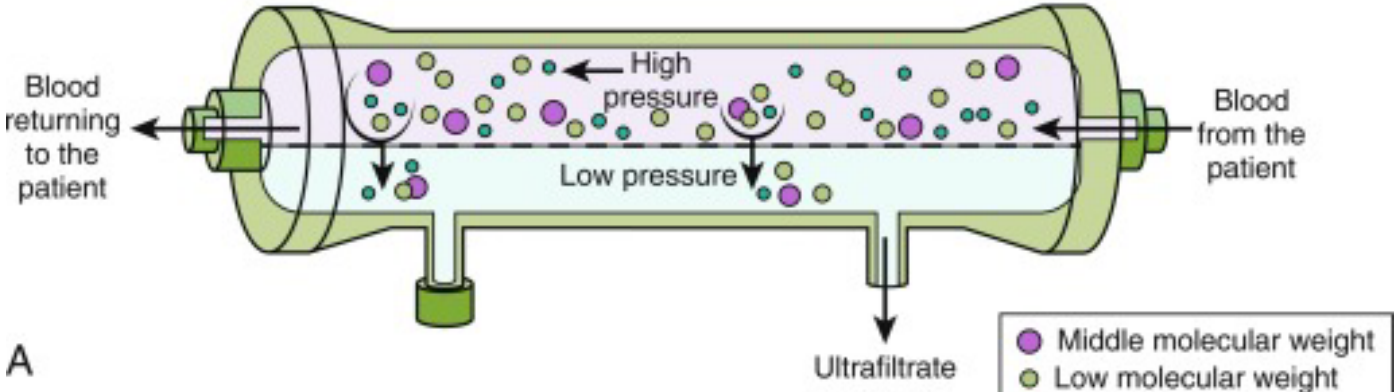


Ronco C., Brendolan A., Bellomo R.: Online Monitoring in continuous renal replacement therapies. Kidney International, Vol 56, Suppl. 72 (1999), pp S-8

Principi di funzionamento

Attraverso la membrana del filtro il trasporto di acqua e soluti avviene sulla base di due principi differenti:

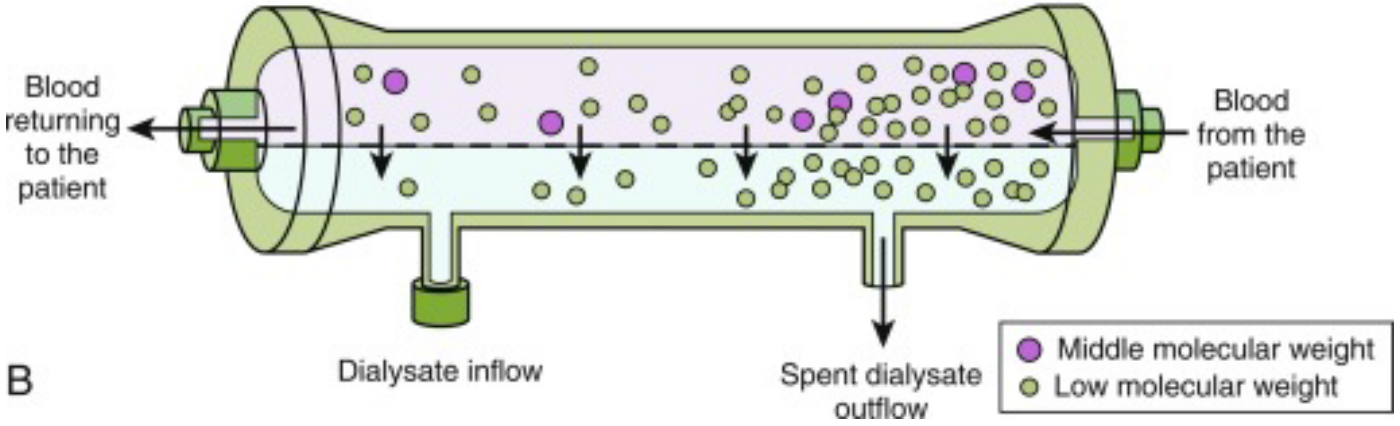
CONVEZIONE



L'acqua plasmatica si sposta per gradiente di pressione (TMP) e «trascina» i soluti

Meccanismo alla base di
ULTRAFILTRAZIONE (SCUF)
EMOFILTRAZIONE (CVVH, CVVHDF)

DIFFUSIONE



I soluti attraversano la membrana per differenza di concentrazione (P osmotica) tra plasma e dialisato

Meccanismo alla base della
DIALISI (CVVHD, CVVHDF)

Reinfusione

1. PERCHE' UNA REINFUSIONE?

- ✓ Per rimpiazzare la grande quantità di UF prodotto (necessaria per clearance dei soluti per convezione)
- ✓ Per permettere una **depurazione plasmatica** per diluizione (UF rimpiazzato da soluzione con composizione simile all'acqua plasmatica «pulita»)

2. QUANDO REINFONDERE?

A. PRE-FILTRO (PRE-DILUIZIONE)

- Minor rischio coagulazione filtro (↓Ht)
- Ridotta eliminazione dei soluti

B. POST-FILTRO (POST-DILUIZIONE)

- Maggiore eliminazione dei soluti
- Maggiore rischio di coagulazione filtro

Preferire PRE-DILUIZIONE se:

- Hct elevato;
- Bassi flussi ematici (per accessi vascolari non ottimali)
- Necessità di alti tassi di filtrazione
- Problemi di coagulazione filtro
- CRRT senza anticoagulante

Prescrizioni standard reinfusione in CVVH:

- Con Eparina: 1/3 reinfusione PRE – 2/3 POST
- Con Citrato: 100% reinfusione POST

Quale metodica scegliere?

CLEARENCE DIFFUSIVA

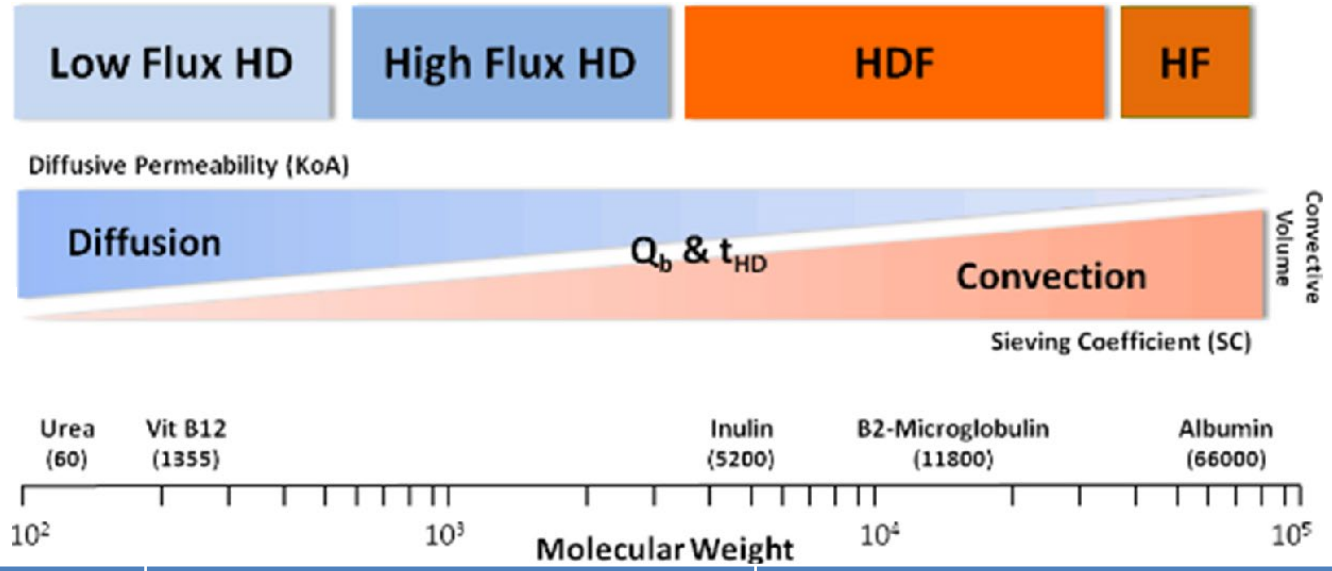
per molecole piccole (< 500 D) e con i flussi tipici della CRRT (Qb 100-200 m/min e Qd 20-30 ml/min) la concentrazione di soluto nel dialisato in uscita è simile a quella nel sangue in entrata

Cl = Qd

CLEARENCE CONVETTIVA

dipende dal coefficiente di Sieving e da Quf (reinfusato)

Cl = Quf x S



Coefficiente di Sieving (S)

è il rapporto tra la concentrazione del soluto nell'ultrafiltrato e quella nell'acqua plasmatica (S=1 per l'urea)

Cosa voglio rimuovere	Esempi	Metodica CRRT
Acqua (18 Da)		**Dialisi** meglio che filtrazione
Molecole piccole (<500 Da)	Elettroliti, ioni H+, creatinina, urea, litio	**Dialisi** (più veloce) o filtrazione
Molecole medie (500-5.000 Da)	Farmaci, vit B12, mioglobina	**Filtrazione** meglio che dialisi
Molecole grandi (5.000-50.000 Da)	Citochine, complemento	**Filtrazione, adsorbimento**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 22, 2009 VOL. 361 NO. 17

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*

METHODS

We randomly assigned critically ill adults with acute kidney injury to continuous renal-replacement therapy in the form of postdilution continuous venovenous hemodiafiltration with an effluent flow of either 40 ml per kilogram of body weight per hour (higher intensity) or 25 ml per kilogram per hour (lower intensity). The primary outcome measure was death within 90 days after randomization.

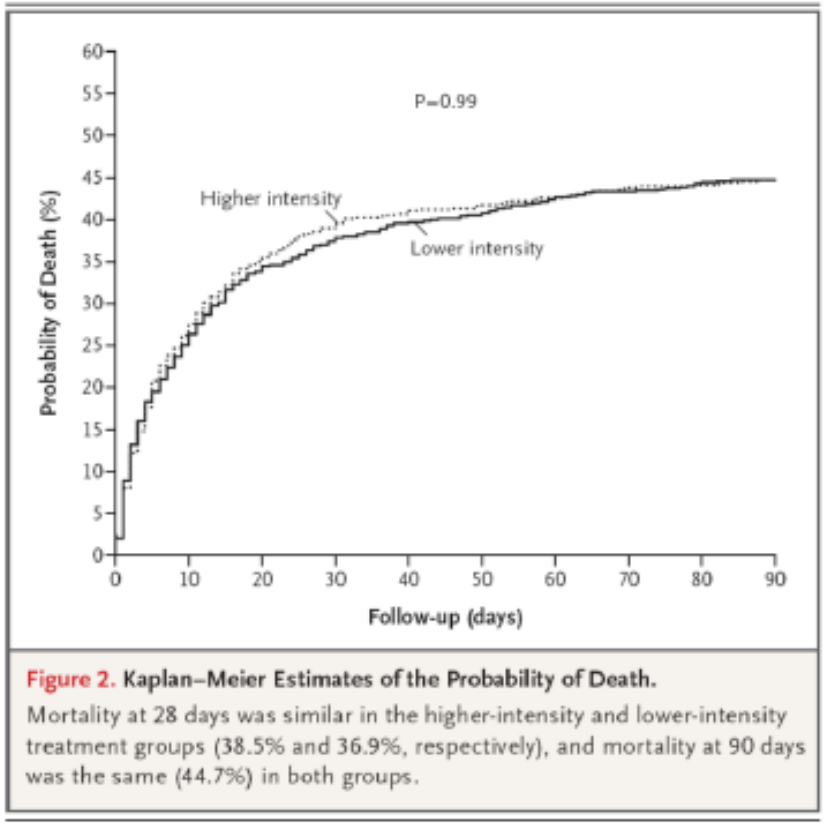


Figure 2. Kaplan–Meier Estimates of the Probability of Death.
Mortality at 28 days was similar in the higher-intensity and lower-intensity treatment groups (38.5% and 36.9%, respectively), and mortality at 90 days was the same (44.7%) in both groups.

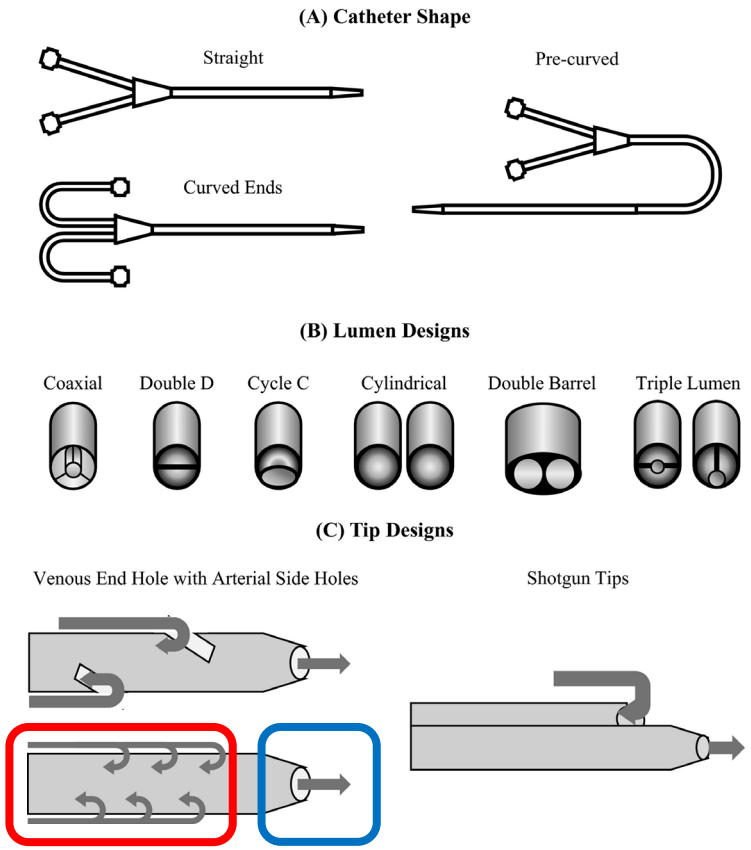
Best practice window: **Q_{EFF} 20-40 ml/kg/h**

Accesso Vascolare

Scelta della sede:

1. Vena giugulare interna dx
2. Vena femorale (dx o sx)
3. Vena giugulare interna sx
4. Vena succlavia (solo brevi periodi → alto rischio stenosi)

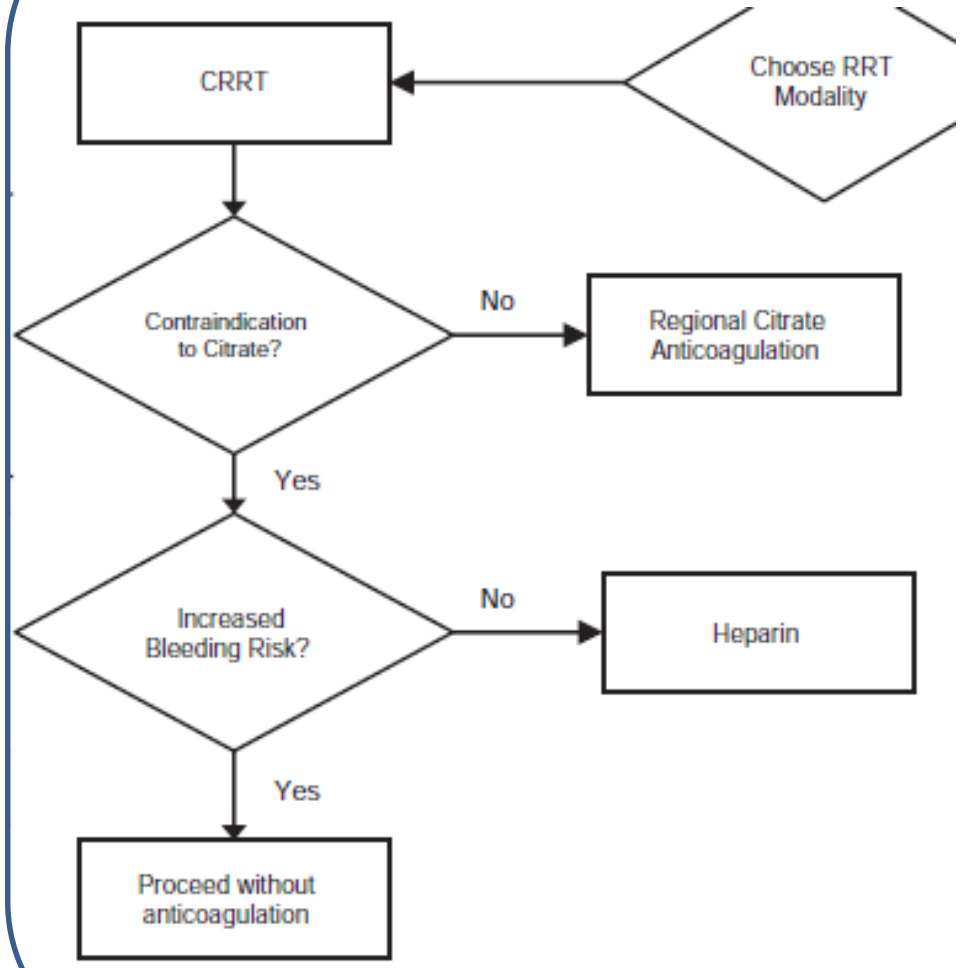
Rischi	v. femorale	v. giugulare	v. succlavia
Infezione	elevata (10,7% dopo 1 settimana)	discreta (5,4 % dopo 3 settimane)	meno frequentemente
Trombosi del vaso	possibile (rischio di Embolia polmonare)	discreta (20%) per lo più asintomatica; sintomatica in presenza di FAVI se la Trombosi interessa v. anonima o v.cava sup.	elevata (50%), sintomatica solo in presenza di FAVI omolaterale
Malfunzionamento	frequente	Poco frequente	Poco frequente



Diametro: 12-14 Fr
Lunghezza: 12-15 cm (VGIdx)
15-20 cm (VGIsx)
≥25 cm (vena femorale)

Anticoagulazione regionale con citrato (RCA)

INDICAZIONI



(Linee guida KDIGO 2012)

CONTROINDICAZIONI

- Insufficienza epatica acuta
- Shock con ipoperfusione severa
- Grave ipossiemia

EVIDENZE

- Rischio emorragico < UFH
- Durata filtro > UFH
- Non differenze di mortalità

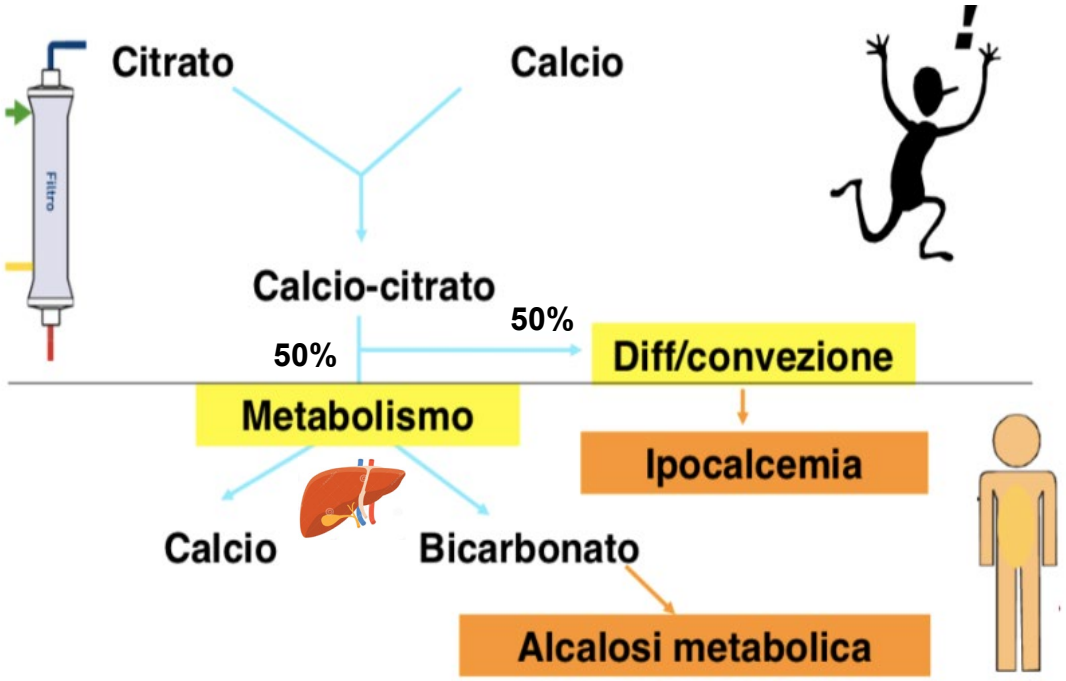
JAMA | Original Investigation

Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury
A Randomized Clinical Trial

RICH (2020)

RCA: Metabolismo del Citrato

Complessi Ca-Citrato non filtrati (≃ 50%) arrivano al pz: **CITRATE LOAD**



STRATEGIE PER ↓ CITRATE LOAD

- ↑ $Q_{R(POST)}$ e/o Q_D per ↑eliminazione
- ↓ $mmol_{CIT}/L_B$ (attenzione a Ca^{++} post!)
- ↓ Q_B (mai <100 ml/min)
- Sostituire filtro se elvata TMP (clogging)

METABOLISMO INSUFFICIENTE
(insufficienza epatica, shock, ipossiemia)

ACCUMULO CA-Citrato

- Acidosi metabolica
- ↓Ca++ ionizzato

SOSPETTA INTOSSICAZIONE CITRATO

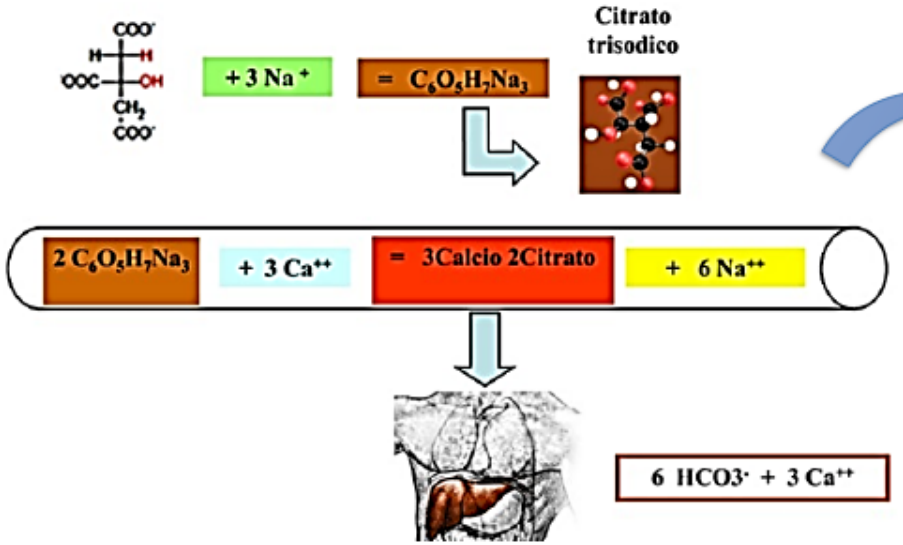
- Acidosi metabolica (pH<7.2 e/o BE<-5)
- ↓ Ca^{++}<1.1 mmol/l
- **Ca_{tot} / Ca^{++} > 2.5**

- **Sospendere RCA**
- **Strategie per ↓ citrate load**

CVVHD con CiCa

Parametri iniziali:

- flusso sangue 100 ml/min
- flusso dialisato 2000 ml/h
- perdita oraria 50-100 ml/h



Sistema Fresenius Ci-Ca CVVHD – effetti metabolici

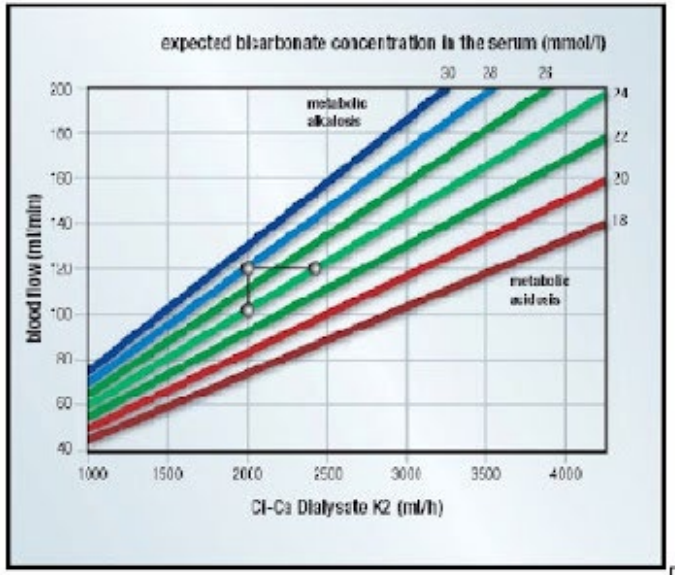


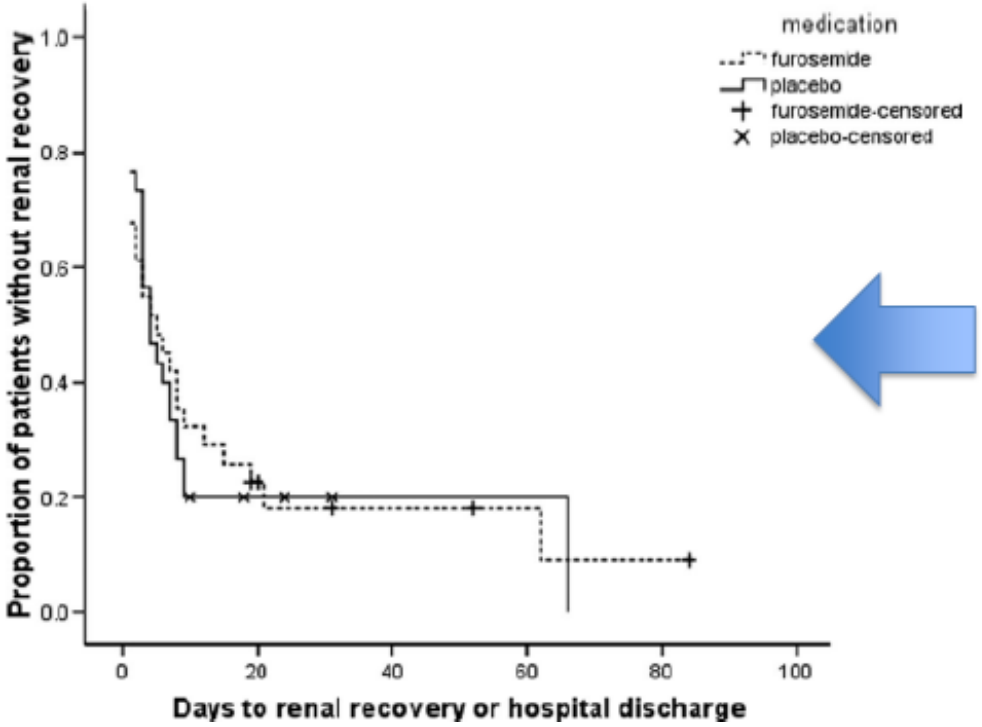
Figura 1

Ca Totale / Ca Ionizzato < 2.1

Interruzione del trattamento

Furosemide does not improve renal recovery after hemofiltration for acute renal failure in critically ill patients: A double blind randomized controlled trial*

«Little is known about the proper time to withdraw CRRT and how to proceed in the recovery phase of ARF. During CRRT, many patients show oliguria or anuria. Because of that, physicians may be tempted to give diuretics when CRRT ends»



70 pz in VM e CVVH x AKI (no CKD)

placebo vs lasix 0.5 mg/kg/h
mantenendo BI in pareggio e PAM > 60 mmHg

(Crit Care Med 2009 Vol. 37, No. 2)

Recommendations regarding renal replacement therapy in patients with acute heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies.	IIb	B	578–580
Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury.	IIa	C	

2016 **2021**

Journal of the American College of Cardiology
© 2007 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 49, No. 6, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2006.07.073

Heart Failure

Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure

Maria Rosa Costanzo, MD, FACC,* Maya E. Guglin, MD, FACC,†

"Unresolved congestion may contribute to high rehospitalization rates»

Trial randomizzato
Multicentrico

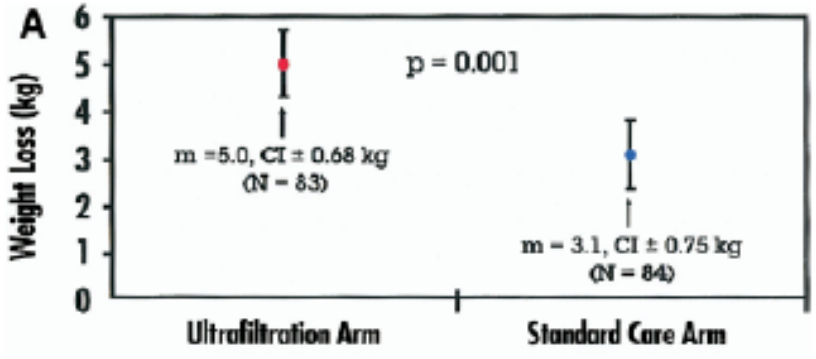
200 Pz con SC e overload
Lasix versus «early UF»

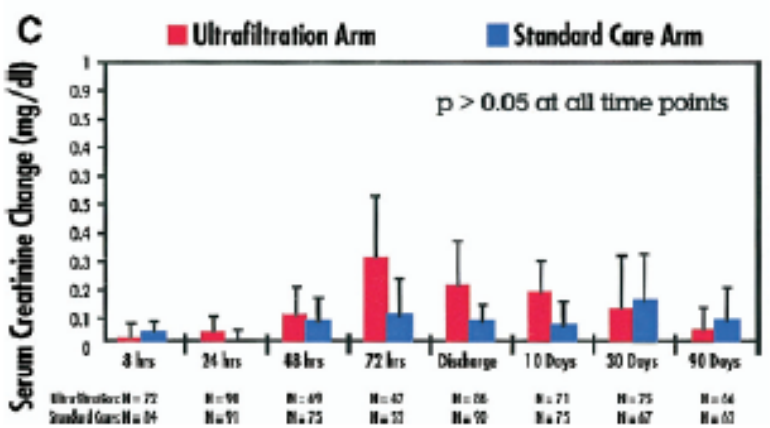
180 ± 120 mg/die

240 ml/h
x 12 ± 12 h

Pz con ≥ 2 segni di congestione, senza SCA o instabilità emodinamica

End point 1° efficacia > CP e Dispnea a 48 h
End point 1° sicurezza > Δ Creat/Urea/QE ed Ipotensione a 48-72 h
End poin 2° > ..., riospedalizzazioni





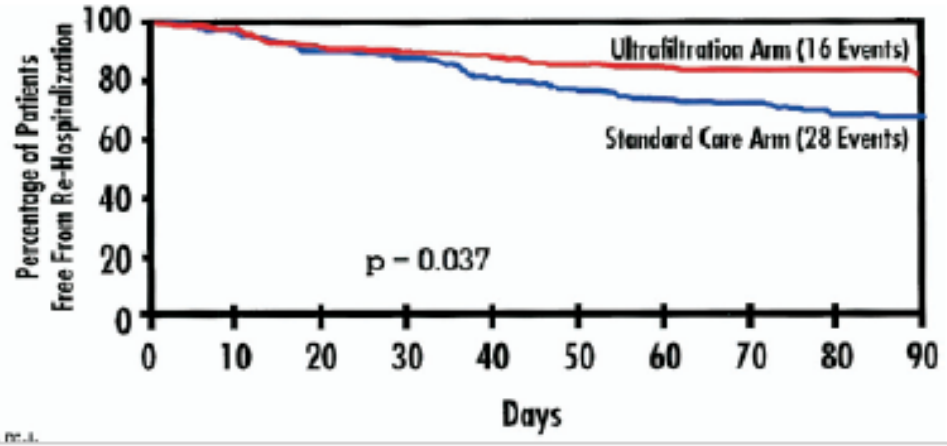
Ipokaliemia 1% vs 12%

RIOSPEDALIZZAZIONE X SC A 3 MESI

?

18% VS 32% (P 0.03)

- Rimozione UF iso-osmotico
- Non attivazione RAAS
- Ripristino sensibilità a lasix



Journal of the American College of Cardiology
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Published by Elsevier Inc.

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Heart Failure

Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure

Maria Rosa Costanzo, MD, FACC,* Maya E. Guglin, MD, FACC,†

Clinical Trial

Continuous Ultrafiltration for Congestive Heart Failure: The CUORE Trial

GIANCARLO MARENZI, MD, FESC,[1] MANUELA MURATORI, MD,[1] EUGENIO R. COSENTINO, MD,[4] ELISA R. RINALDI, MD,[3] VALERIA DONGHI, MD,[1] VALENTINA MILAZZO, MD,[1] EMILIANA FERRAMOSCA, MD,[3] CLAUDIO BORGHI, MD,[4] ANTONIO SANTORO, MD,[3] AND PIERGIUSEPPE AGOSTONI, MD, PhD, FESC[1,2]

Milan and Bologna, Italy

ORIGINAL ARTICLE

Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

Bradley A. Bart, M.D., Steven R. Goldsmith, M.D., Kerry L. Lee, Ph.D., Michael M. Givertz, M.D., Christopher M. O'Connor, M.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Martin M. LeWinter, M.D., Elizabeth O. Ofili, M.D., M.P.H., Lynne W. Stevenson, M.D., Marc J. Semigran, M.D., G. Michael Felker, M.D., Horng H. Chen, M.D., Adrian F. Hernandez, M.D., Kevin J. Anstrom, Ph.D., Steven E. McNulty, M.S., Eric J. Velazquez, M.D., Jenny C. Ibarra, R.N., M.S.N., Alice M. Mascette, M.D., and Eugene Braunwald, M.D., for the Heart Failure Clinical Research Network

FOCUS ISSUE: CLINICAL TRIALS AND REGISTRIES

Aquapheresis Versus Intravenous Diuretics and Hospitalizations for Heart Failure

Maria Rosa Costanzo, MD,[a] Daniel Negoianu, MD,[b] Brian E. Jaski, MD,[c] Bradley A. Bart, MD,[d] James T. Heywood, MD,[e] Inder S. Anand, MD, DPhil (Oxon),[f] James M. Smelser, MD,[g] Alan M. Kaneshige, MD,[h] Don B. Chomsky, MD,[i] Eric D. Adler, MD,[j] Garrie J. Haas, MD,[k] James A. Watts, MD,[l] Jose L. Nabut, MS,[m] Michael P. Schollmeyer, DVM,[m] Gregg C. Fonarow, MD[n]

IJC Metabolic & Endocrine 2 (2014) 19–25

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The impact of ultrafiltration in acute decompensated heart failure: A systematic review and meta-analysis ☆☆

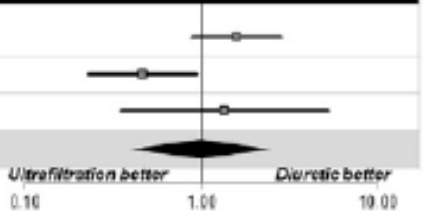
Nader Makki [a,*], Seth Maliske [a], Amy Blevins [a], Saket Girotra [a], Peter Cram [b,c]

All-cause mortality

Study	Year	Hazard ratio [confidence interval]	Hazard ratio & 95% CI
Badawy	2012	0.53 [0.13-2.19]	
Bart	2005	1.25 [0.34-4.65]	
Bart	2012	1.40 [0.63-3.15]	
Costanza	2011	0.80 [0.32-2.02]	
Hanna	2012	0.87 [0.18-4.16]	
Overall		**0.99 [0.60-1.61]**	

Re-hospitalization for any cause

Study	Year	Hazard ratio [confidence interval]	Hazard ratio & 95% CI
Bart	2012	1.58 [0.88-2.84]	
Costanza	2011	0.46 [0.23-0.93]	
Hanna	2012	1.33 [0.35-5.16]	
Overall		**0.96 [0.39-2.35]**	



Recommendations regarding renal replacement therapy in patients with acute heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies.	IIb	B	578–580
Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury.	IIa	C	

2016 **2021**

Importanza della DECONGESTIONE!

ESC
European Society of Cardiology

CIN

Recommendations for the prevention of contrast-induced nephropathy

Recommendations	Dose	Class[a]	Level[b]
Patients undergoing coronary angiography or MSCT			
It is recommended that all patients are assessed for the risk of contrast-induced nephropathy.		I	C
Adequate hydration is recommended.		I	C
Patients with moderate or severe CKD (National Kidney Foundation stages 3b and 4)			
Use of low-osmolar or iso-osmolar contrast media is recommended.[284–286]		I	A
It is recommended that the volume of contrast media be minimized.[287,288]	Total contrast volume/GFR <3.7.[c]	I	B
In statin-naïve patients, pre-treatment with high-dose statins should be considered.[293]	Rosuvastatin 40/20 mg or atorvastatin 80 mg.	IIa	A
Pre- and post-hydration with isotonic saline should be considered if the expected contrast volume is >100 mL.	1 mL/kg/h 12 h before and continued for 24 h after the procedure (0.5 mL/kg/h if LVEF ≤35% or NYHA >2).	IIa	C
As an alternative to the pre- and post- hydration regimen, tailored hydration regimens[d] may be considered.[295–297]		IIb	B
Patients with severe CKD (National Kidney Foundation stage 4)			
Prophylactic haemofiltration 6 h before complex PCI may be considered.[298–300]	Fluid replacement rate 1000 mL/h without negative loss and saline hydration continued for 24 h after the procedure.	IIb	B
Haemodialysis is not recommended as a preventive measure.[300,301]		III	B

2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Prevention of Radiocontrast-Agent–Induced Nephropathy by Hemofiltration

Giancarlo Marenzi, M.D., Ivana Marana, M.D., Gianfranco Lauri, M.D., Emilio Assanelli, M.D., Marco Grazi, M.D., Jeness Campodonico, M.D., Daniela Trabattoni, M.D., Franco Fabbiocchi, M.D., Piero Montorsi, M.D., and Antonio L. Bartorelli, M.D.

The American Journal of Medicine (2006) 119, 155-162

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THE AMERICAN JOURNAL of MEDICINE®

CLINICAL RESEARCH STUDY

Comparison of Two Hemofiltration Protocols for Prevention of Contrast-induced Nephropathy in High-risk Patients

Giancarlo Marenzi, MD, Gianfranco Lauri, MD, Jeness Campodonico, MD, Ivana Marana, MD, Emilio Assanelli, MD, Monica De Metrio, MD, Marco Grazi, MD, Fabrizio Veglia, PhD, Franco Fabbiocchi, MD, Piero Montorsi, MD, Antonio L. Bartorelli, MD

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Conclusioni

- CRRT come presidio per equilibrare omeostasi finché malattia di base è guarita: non aumenta probabilità di guarigione, né del paziente né del rene, ma aiuta a mantenerle in vita il paziente e preserva funzione di altri organi finché il sistema recupera

- Salvo urgenze dialitiche e specifici contesti delicati, atteggiamento attendistico nell'avviare CRRT può essere preferibile → APPROCCIO SEQUENZIALE, guidato dall'emodinamica

- Meglio le metodiche continue, metodiche diffusive e convettive sono sovrapponibili, la dose è «indifferente» entro certi limiti

- Al di là del metodo utilizzato, la decongestione è fondamentale

Prescrizione del trattamento (I)

1. **TECNICA DI CRRT (SCUF – CVVH – CVVHD – CVVHDF):** in base a molecole da rimuovere

2. **ULTRAFILTRAZIONE NETTA (UF_{NET}):** bilancio negativo dei fluidi in ingresso e uscita dal circuito

   CVVH: Q_{UF}-Q_R CVVHD: $Q_{D(OUT)} - Q_{D(IN)}$ CVVHDF: $[Q_{D(OUT)}+Q_{UF}] – [Q_{D(IN)} + Q_R]$

3. **FRAZIONE DI FILTRAZIONE (FF):** % acqua plasmatica filtrata nell'unità di tempo (solo per convettive)

   $FF=Q_{UF}/Q_B$ → mantenere **<20-25%** per evitare eccessiva emoconcentrazione e coagulazione filtro!

   NB: se necessario Q_{UF} molto elevato per rapida rimozione di piccoli soluti meglio utilizzare metodiche diffusive, non vincolate da FF

4. **MEMBRANA DEL FILTRO**

   - Materiale (polimeri naturali vs sintetici)
   - Coefficiente di ultrafiltrazione (K_{UF}): determina velocita filtrazione e dimensioni molecole filtrate
   - Cut off (massimo peso molecolare filtrato) e retenion onset (peso del soluto interamente filtrato)
     Generalmente retention onset=2 Kd (vitB12) e cut-off=20 Kd (Bence-Jones)

Prescrizione del trattamento (II)

5. DOSE DIALITICA

I flussi di emofiltrazione ed emodialisi («effluente» o Q_{EFF}) determinano la clearance dei soluti.
Prescrizione della dose dialitica = prescrizione Q_{EFF}, tenendo conto che:

- Metodiche convettive (CVVH, dove $Q_{EFF}=Q_{UF}$): mantenere FF<20-25%
- Metodiche diffusive (CVVHD, dove $Q_{EFF}=Q_{D(OUT)}$): relazione lineare tra flusso dialisato e clearance finchè $Q_B/Q_D<0,3$

Best practice window: **Q_{EFF} 20-40 ml/kg/h**

NB: discrepanza dose prescritta-somministrata fino al 15% →sovraprescrivere per compensare down-time!

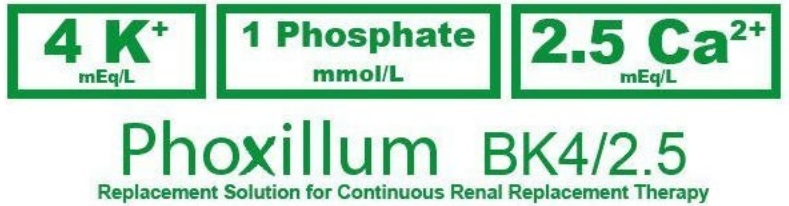
6. LIQUIDI SOSTITUZIONE (diffusive) / REINFUSIONE (convettive) E REINFUSIONE PRE vs POST

7. ANTICOAGULAZIONE

Liquidi di sostituzione e soluzioni dializzanti

Caratteristiche comuni:
- ✓ Composizione simile ai fluidi extracellulari (eccetto K+ e fosforo)
- ✓ Contengono soluzioni tampone per correggere acidosi metabolica
- ✓ Sterili

Scelta della soluzione in base alla composizione:



After reconstitution, A + B

	Calcium Ca^{2+}	Magnesium Mg^{2+}	Sodium Na^{+}	Chloride Cl^{-}	Bicarbonate HCO_3^{-}	Potassium K^{+}	Phosphate HPO_4^{2-}	Dextrose
mmol/L	1.25	0.75	140	114.5	32	4.0	1	0
mEq/L	2.5	1.5	140	114.5	32	4.0	(1 mmol/L)	(0 mg/dL)

Theoretical osmolarity: 294 mOsm/L pH: 7.0 – 8.5

1. Elettrolitica:
   - Na+: isotoniche (140 mmol/L) vs ipotoniche (133 mmol/L)
   - K^{+}: variabile (2-4 mmol/L a seconda delle necessità)
   - Mg^{+}: ai limiti inferiori dei normali valori plasmatici (0.5-0.75 mmol/L)
   - **Ca^{++}: deve essere ASSENTE in liquido di dialisi se anticoagulazione con calcio-citrato** (concessa bassa concentrazione solo in reinfsione post-diluizione)
   - Fosfato: in alcune soluzioni di reinfusione per il trattamento dell'ipofosfatemia

2. Soluzione tampone
   - **Bicarbonato:** tampone più fisiologico. Usare concentrazioni ridotte (HCO3 20 mmol/l) durante citrato
   - **Lattato:** convertito in HCO3 a livello epatico e muscolare. Non usare se insuff epatica/iperlattacidemia
   - Acetato: convertito in HCO3 a livello epatico e muscolare. Poco usato (instabilità di circolo).