PCI στους νεφροπαθείς

ΓΡΑΪΔΗΣ ΧΡΗΣΤΟΣ

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Θεσσαλονίκη

CKD clearly represents a major public heath problem

✓Current estimates from the U.S. ***show that 13% of the population has CKD***, with 341,000 on chronic dialysis and 140,000 with kidney transplants

✓***World-wide, 5-10% of the world's population may also have CKD***, a staggering 300-600 million people

✓***It causes a huge economic burden worldwide.*** Health costs of treating people with CKD are nearly 3-fold higher than those for people without CKD, and the cost of treating ESRD is 10-fold higher

Chronic Kidney Disease (CKD): A silent epidemic

Earlier stage CKD

- **CKD is "under-diagnosed" and "under-treated"**
- **The adverse outcomes of CKD can be prevented or delayed through interventions during earlier stages of CKD**

How to Assess Renal Function?

Abbreviated Modification of Diet in Renal Disease equations (MDRD) equation:

eGFR, ml/min/1.73 m^2= 186 x (Serum Creatinine [mg/dL]) -1.154 x (Age-0.203x (0.742 if female) x (1.210 if African American)

Cockcroft-Gault equation:

$$\text{Creatinine Clearance, ml/min} = \frac{(140 - \text{age}) \times \text{Body Weight [kg]}^*}{\text{Serum Creatinine mg/dL]} \times 72}$$

* Multiple by 0.8 in female

❖ Estimates of GFR are the best overall indices of the level of kidney function

❖ ***The serum creatinine concentration alone should not be used to assess the level of kidney function***

Why Estimate GFR From SCr, Instead of Using SCr for Kidney Function?

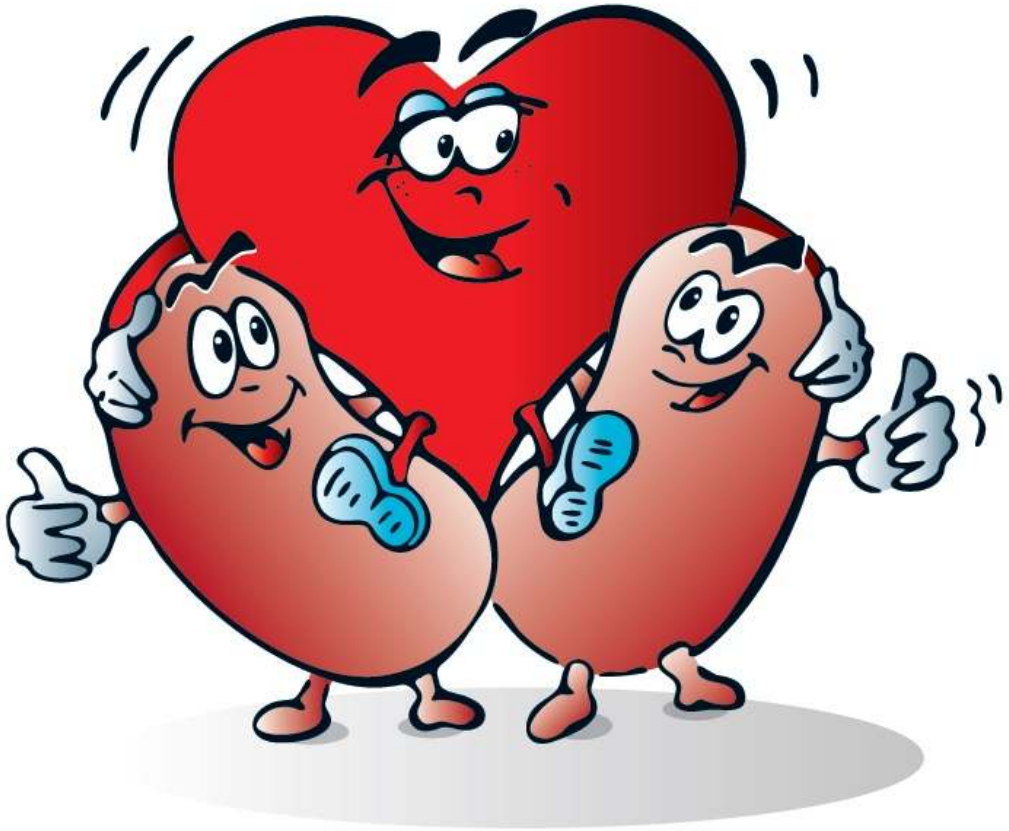
Age	Gender	Race	SCr (mg/dL)	eGFR (mL/min/1.73 m²)	CKD Stage
20	M	B*	1.3	91	1
20	M	W†	1.3	75	2
55	M	W	1.3	61	2
20	F	W	1.3	56	3
55	F	B	1.3	55	3
50	F	W	1.3	46	3

Criteria

1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either:*
   - Pathological abnormalities; or
   - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. eGFR<60 mL/min/1.73m^2 for ≥ 3 months, with or without kidney damage

Stage	Description	GFR (mL/min/1.73 m²)		Action
1 (LOW)	Kidney damage with normal or ↑ GFR	≥90	PATIENT EDUCATION	Confirm diagnosis of CKD; Initiate measures to slow progression and reduce CVD risk
2 (GUARDED)	Kidney damage with mild ↓ GFR	60-89		Estimate progression
3 (ELEVATED)	Moderate ↓ GFR	30-59		Evaluate and treat complications of CKD
4 (HIGH)	Severe ↓ GFR	15-29		Prepare for kidney replacement therapy (transplant, dialysis)
5 (SEVERE)	Kidney failure (ESRD)	<15 (or dialysis)		Start kidney replacement therapy

Heart and Kidneys : a complicated love story



The multiple connections that exist between the cardiovascular system and the kidney lead to a complex cardiovascular and renal medicine relationship.

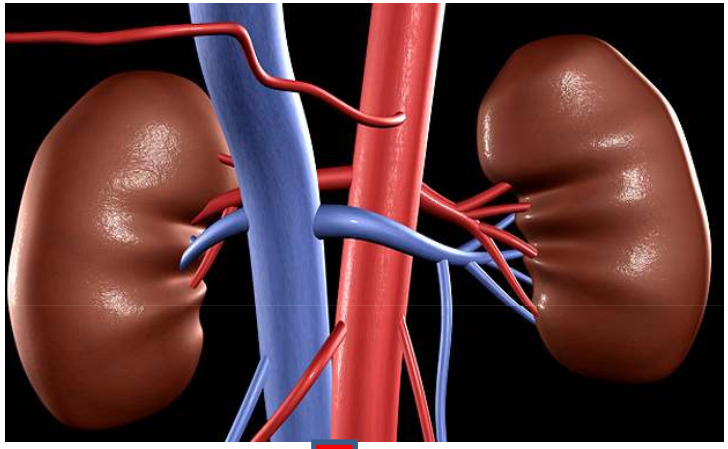
Bidirectional nature of heart-kidney interactions

primary disorders of one organ causing secondary dysfunction or injury to the other

PHYSICAL

CHEMICAL

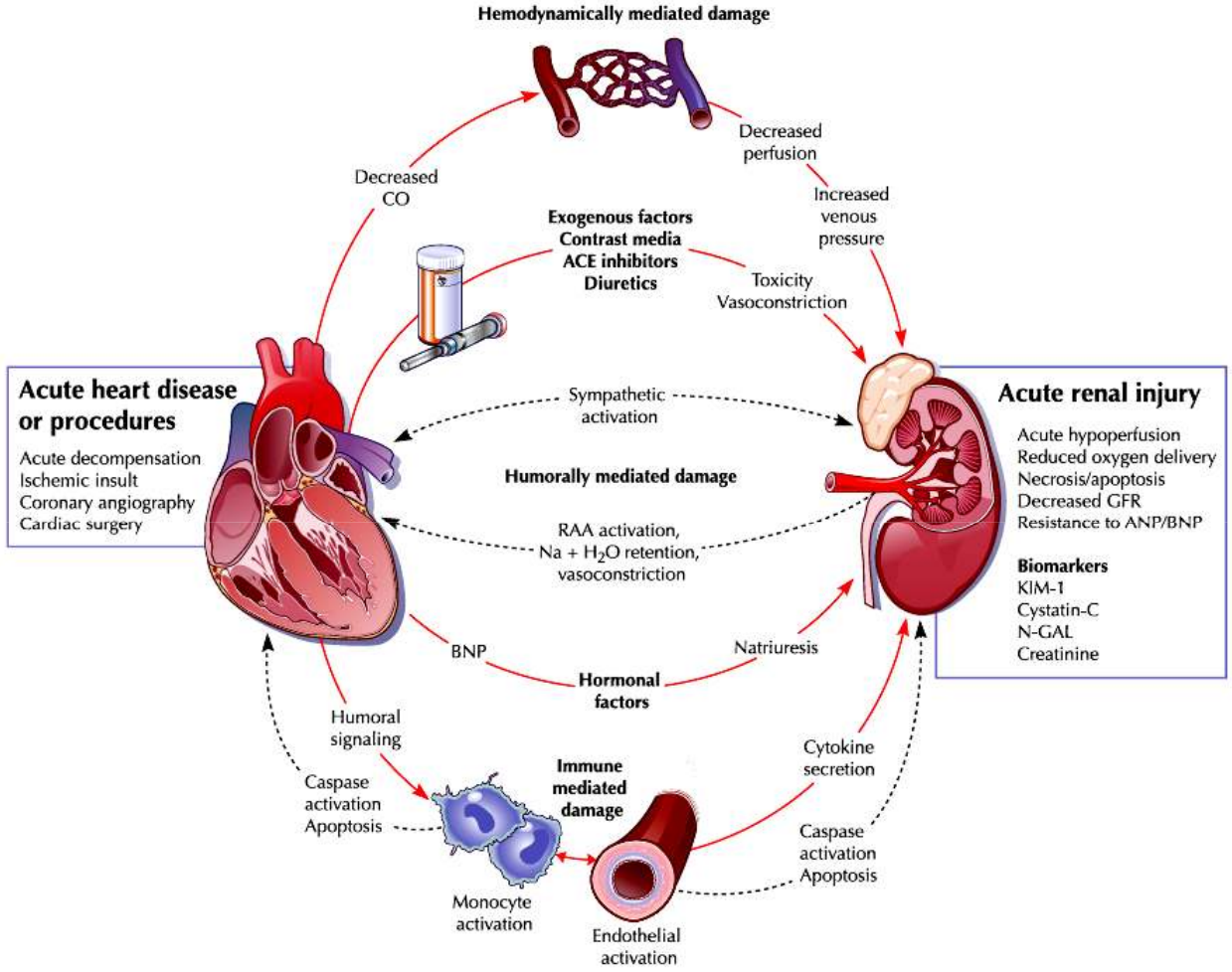
BIOLOGICAL



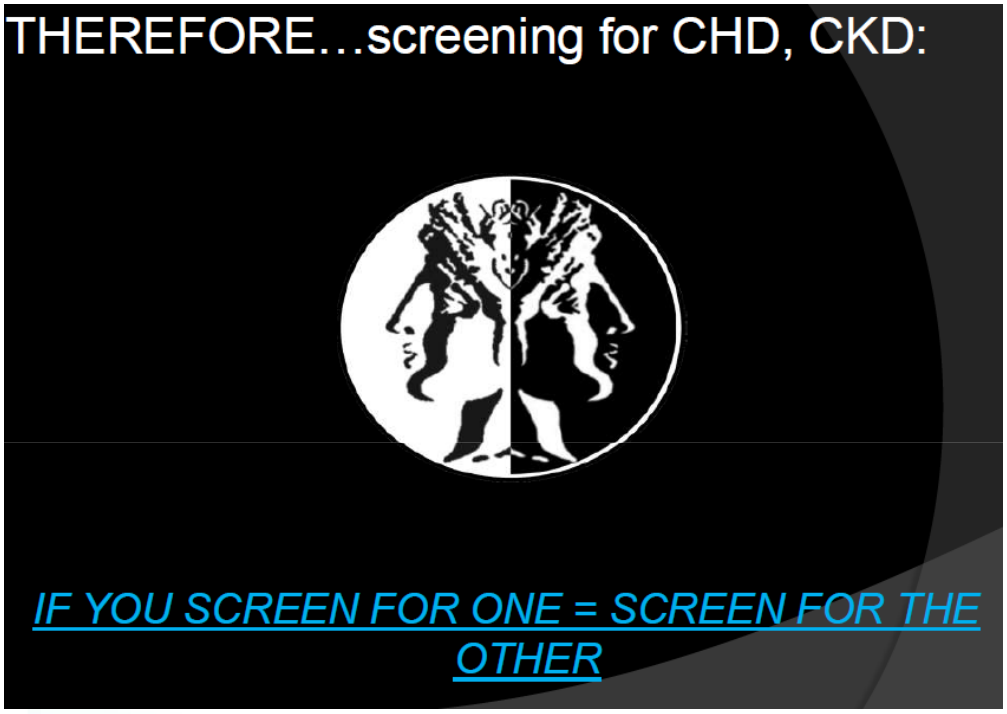
Acute Renal Failure and Death in the Cardiac Patient

Myocardial Infarction, Heart Failure, Arrhythmias, and Cardiac Death in the Renal Patient

The multiple connections that exist between the cardiovascular system and the kidney lead to a complex cardiovascular and renal medicine relationship.



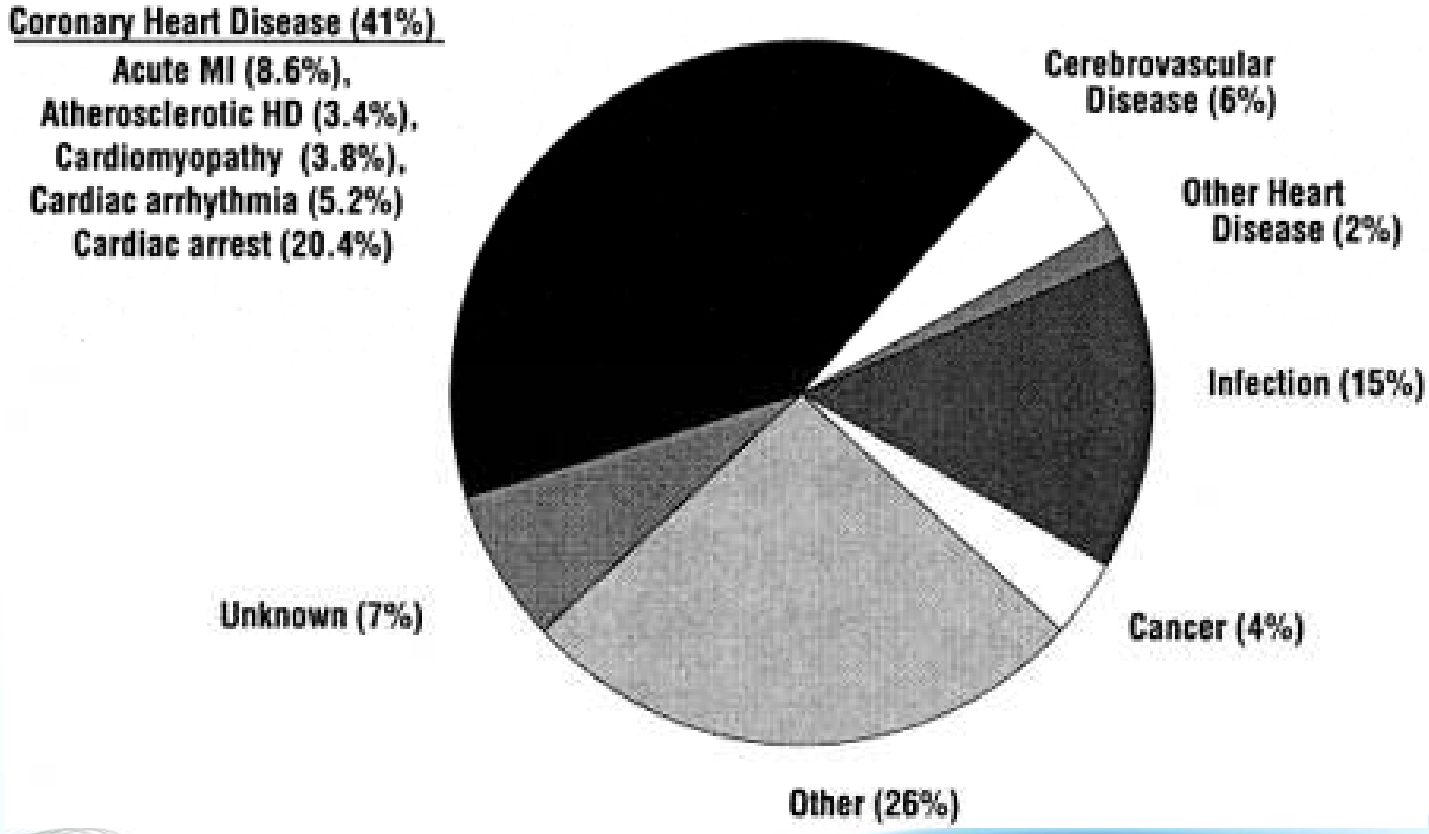
ACC/AHA and National Kidney Foundation recommend that *CKD should be considered as equivalent of CAD*



The prevalence of CVD in the CKD population ranges between 7 and 85% according to the CKD stage and type

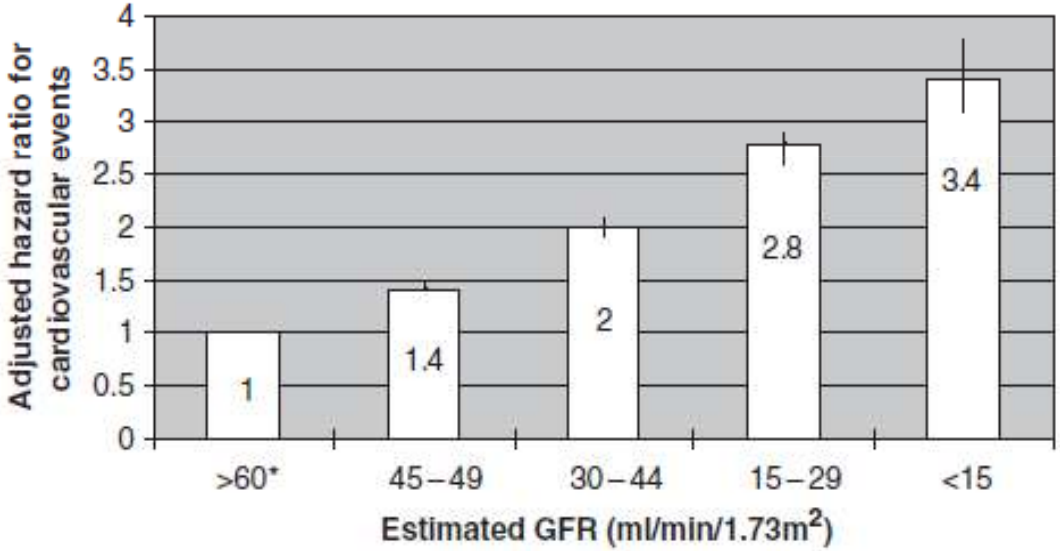
- **The prevalence of CKD is even higher among patients with cardiovascular disease**
  - **14.5% to 42.9% of patients with NSTEMI have moderate to severe CKD**
  - **20% of patients undergoing coronary angiography have stage≥ 3 CKD**

Cardiovascular disease remains the leading cause of mortality in patients with chronic kidney disease (CKD) and dialysis-dependent renal disease.



Death from cardiac causes is 10-20 times more common in chronic kidney disease (CKD) patients than in age- and gender- matched population.

In a large US community study involving over one million people, ***an independent, graded relationship*** was observed between estimated glomerular filtration rate (eGFR) and rates of death, cardiovascular events and hospitalization

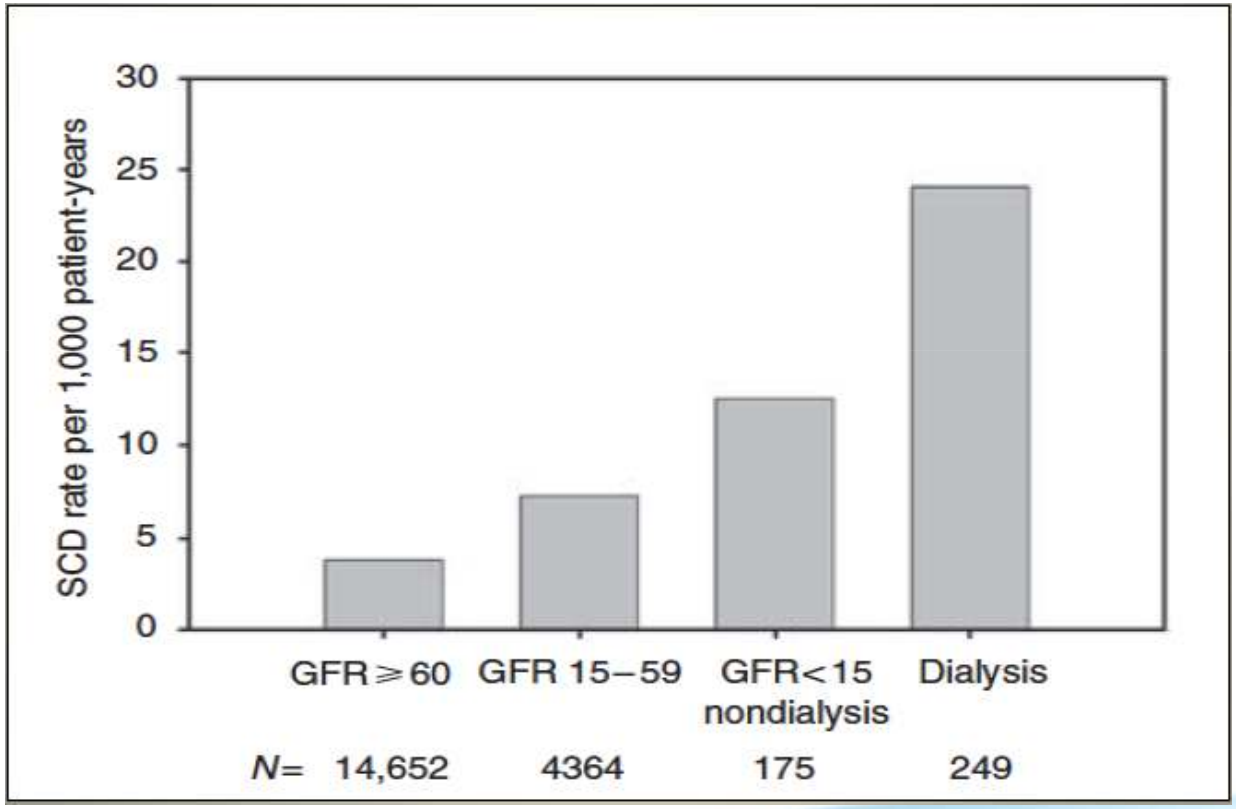


Although patients on dialysis are at greatest risk, the increased risk also extends to those with milder forms of CKD

Adjusted Hazard Ratio for Cardiovascular Events among 1 120 295 adults according to estimated glomerular filtration rate (eGFR). Adapted from Go et al.5

Rates Sudden Cardiac Death by GFR

- Sudden cardiac death (SCD) constitutes 62% of the CV mortality in ESRD and 25% of all-cause mortality.
- The annual rate of SCD in ESRD patients on dialysis is 7%



Kidney International 2009; 76: 652–658

In chronic kidney disease patients who are not hemodialysis dependent, the risk of dying of cardiovascular disease is greater than the risk of developing ESRD.

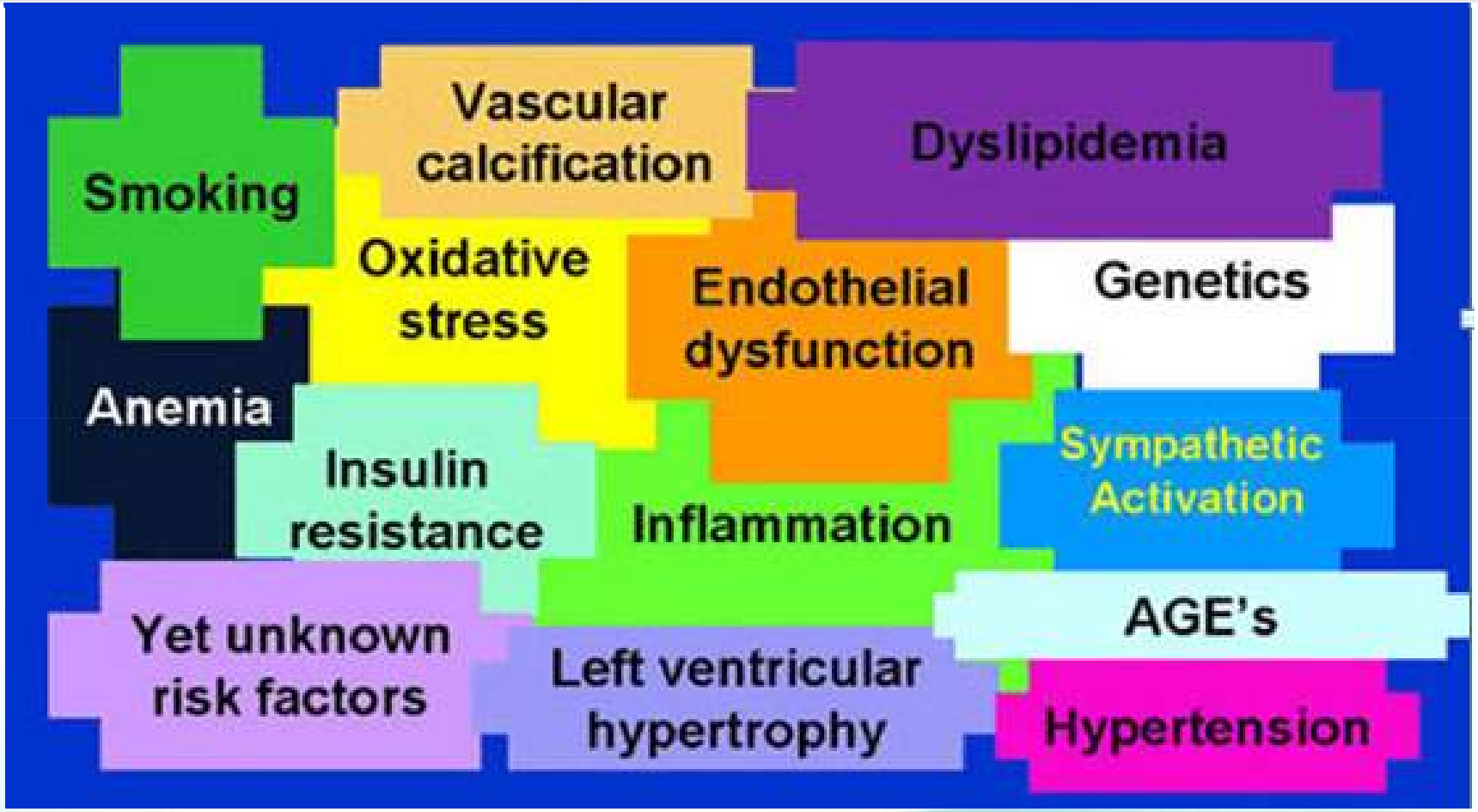
Outcomes of 27,998 patients with evidence of CKD

End Points	GFR, 60-89; No Proteinuria (n = 14 202)	Stage 2 GFR, 60-89; Proteinuria (n = 1741)	Stage 3 GFR, 30-59 (n = 11 278)	Stage 4 GFR, 15-29 (n = 777)
Disenrolled from plan	14.9	16.2	10.3	6.6
Died (prior to transplant/dialysis)	10.2	19.5	24.3	45.7
Received a transplant	0.01	0.2	0.2	2.3
Initiated dialysis	0.06	0.9	1.1	17.6
None of the above through June 30, 2001	74.8	63.3	64.2	27.8

That the 5-year mortality rates for CKD stages 2, 3, and 4 were 19.5, 24.3, and 45.7% respectively; while the percentages of patients with these stages who progressed to ESRD were much lower at 1.1%, 1.3%, and 19.9%.

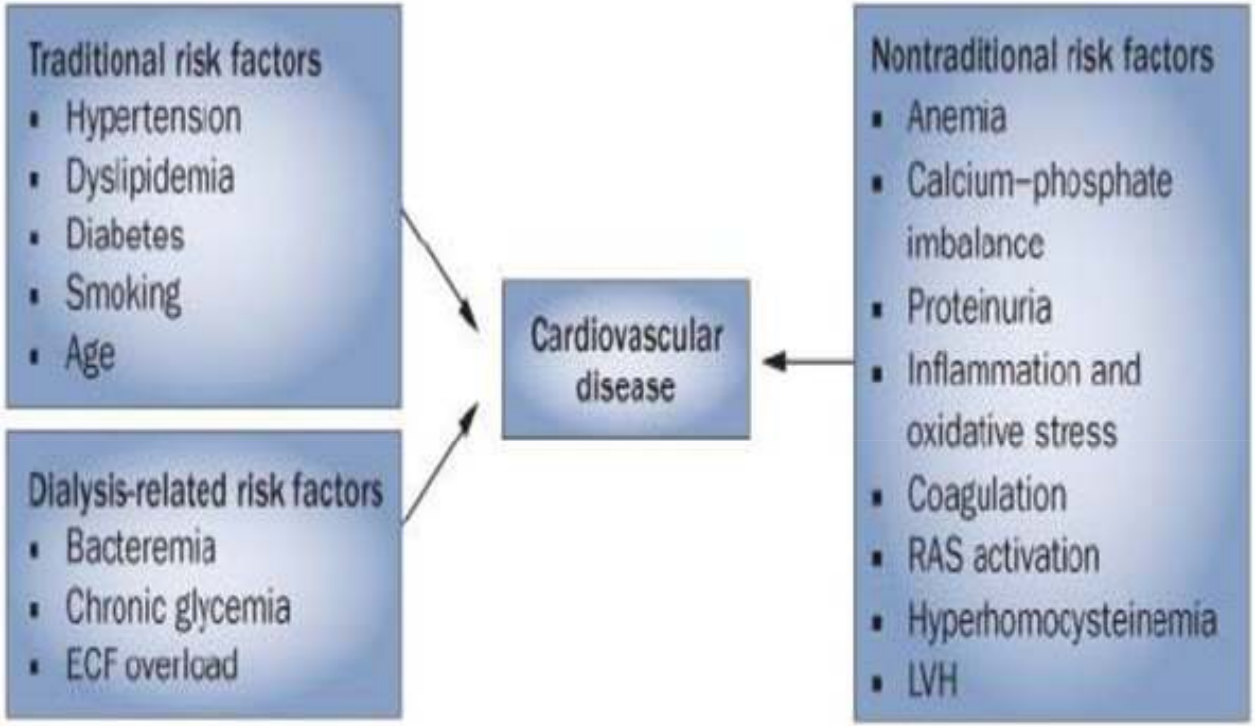
Arch Intern Med. 2004;164:659-663

Causes of cardiovascular diseases in CKD: A puzzle with many pieces



Unique Cardiac Risk Factors in CKD

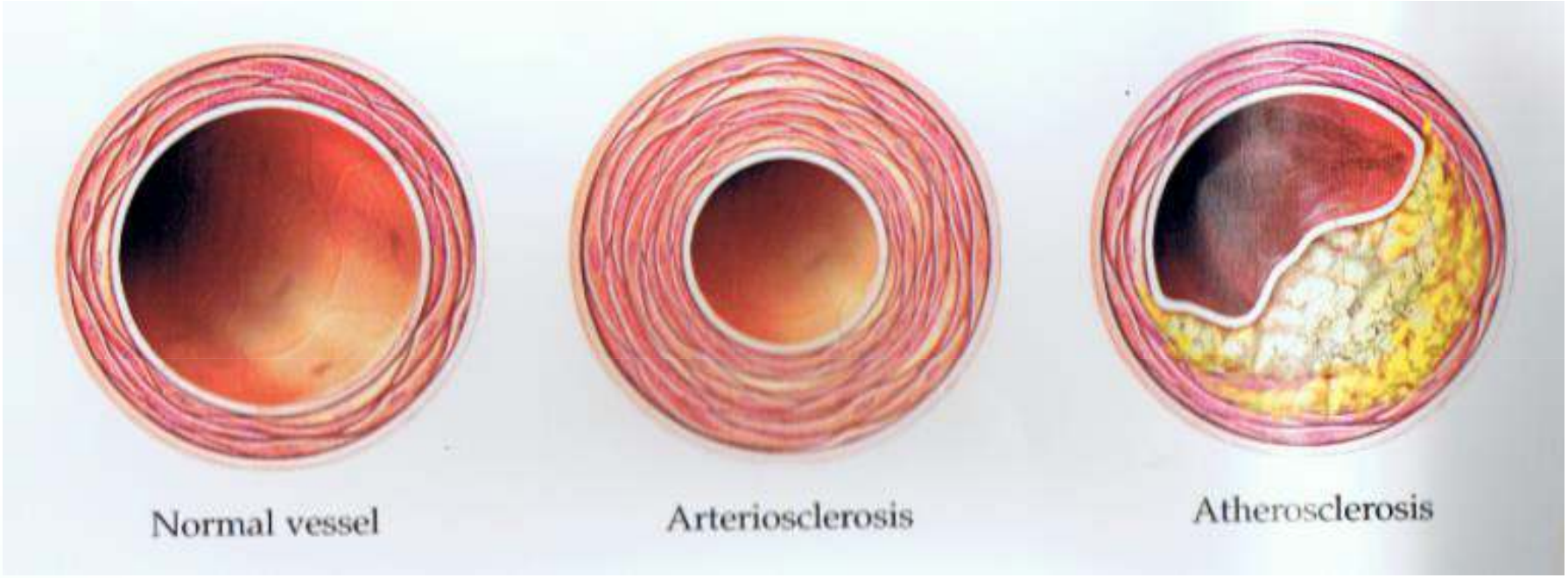
Standard cardiovascular risk factors are common in CKD, *but do not fully explain* the high incidence of cardiovascular events or increased mortality rates



This disproportionate impact of cardiovascular events on patients with renal disease *is due to the exceptionally atherogenic environment* created by a combination of classical risk factors with other, novel factors

Arteriosclerosis and Atherosclerosis

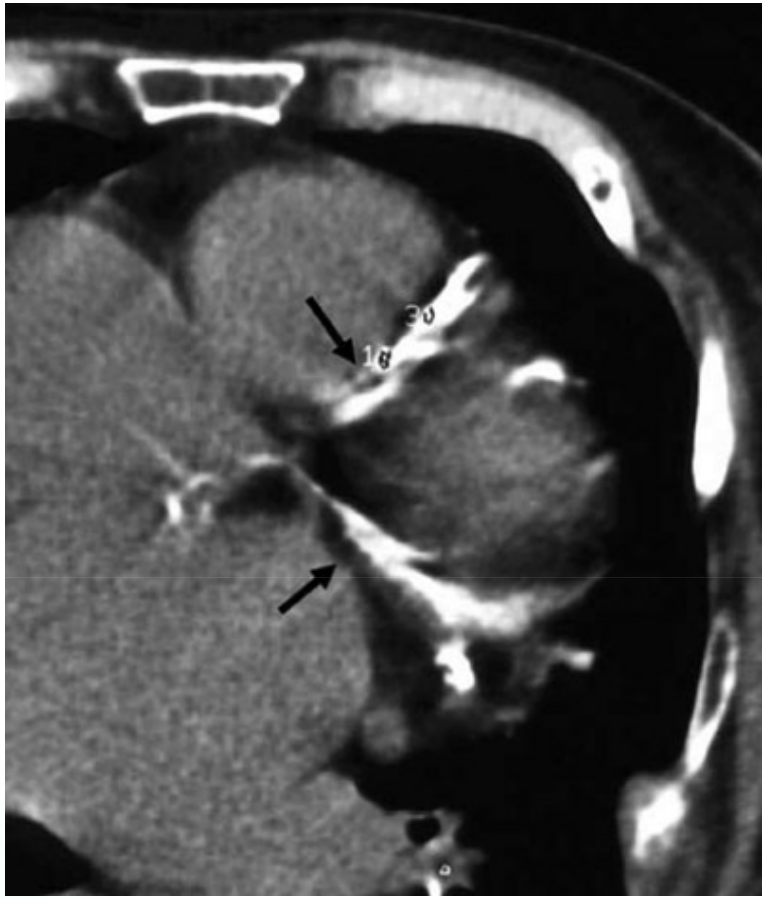
The vascular complications in CKD are attributable to two different but associated mechanisms, namely atherosclerosis and arteriosclerosis.



✓**Atherosclerosis is an intimal disease that (in the general population) is characterized by fibroatheromatous plaques and occlusive disease.**

✓**The other characteristic feature in CKD is thickening and calcification of the medial arterial layer known as 'arteriosclerosis'.**

Coronary Calcification in Chronic Kidney Disease



CT of a patient with chronic renal failure under haemodialysis

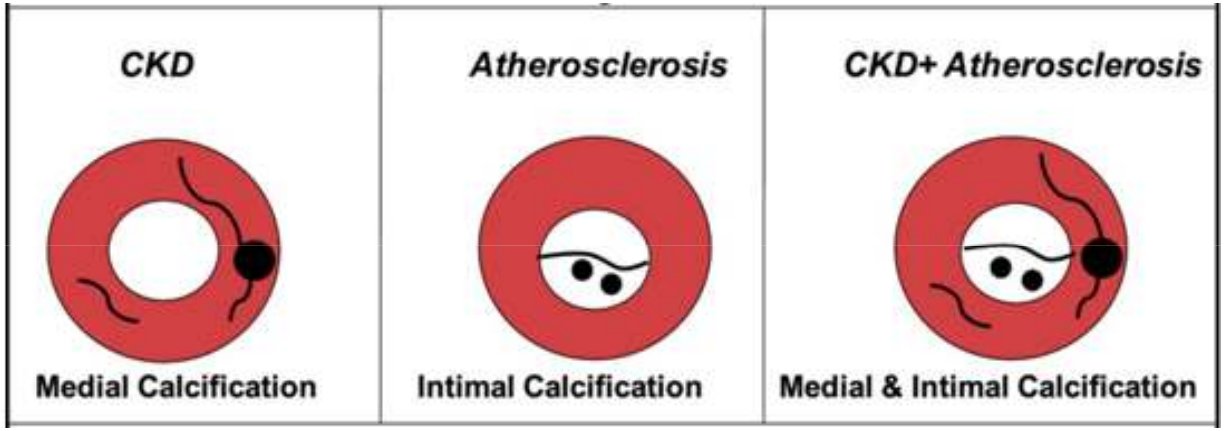
CAC is frequently seen in patients with all stages of CKD

Coronary Calcification in Patients with Chronic Kidney Disease and Coronary Artery Disease

Satoko Nakamura, Hatsue Ishibashi-Ueda, Sinichiro Niizuma, Fumiki Yoshihara, Takeshi Horio, and Yuhei Kawano

CJASN
Clin J Am Soc Nephrol
4: 1892–1900, 2009

- **In the non-CKD setting, *CAC deposition is limited almost entirely to the vessel intima* in association with atherosclerosis.**
- ***In CKD, calcification is thought to be both intimal and medial***



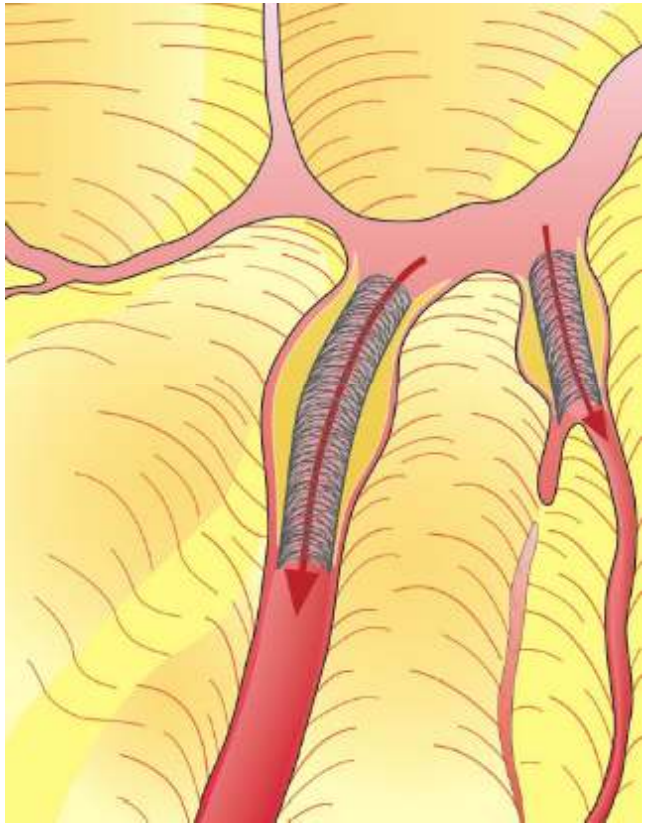
- ***Medial calcification was present only in those with estimated GFR< 30 ml/min per 1.73 m2 and hemodialysis cases*, with incidence increased by the presence of uremic risk factors**
  - **Medial calcification was present in coronary segments that often also contained intimal calcification.**

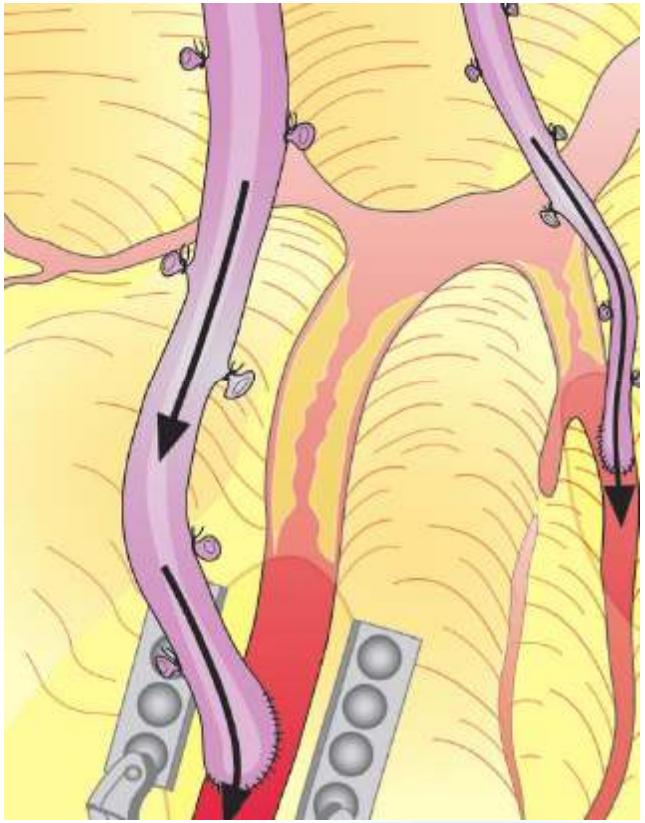
REVASCULARIZATION for Coronary artery disease in CKD or ESRD

In spite of those statistics, dialysis patients and patients with CKD that does not require dialysis are significantly less likely than patients with normal renal function to undergo coronary angiography and revascularization

REVASCULARIZATION for Coronary artery disease in CKD or ESRD

To treat or not to treat ?





REVASCULARIZATION for Coronary artery disease in CKD or ESRD

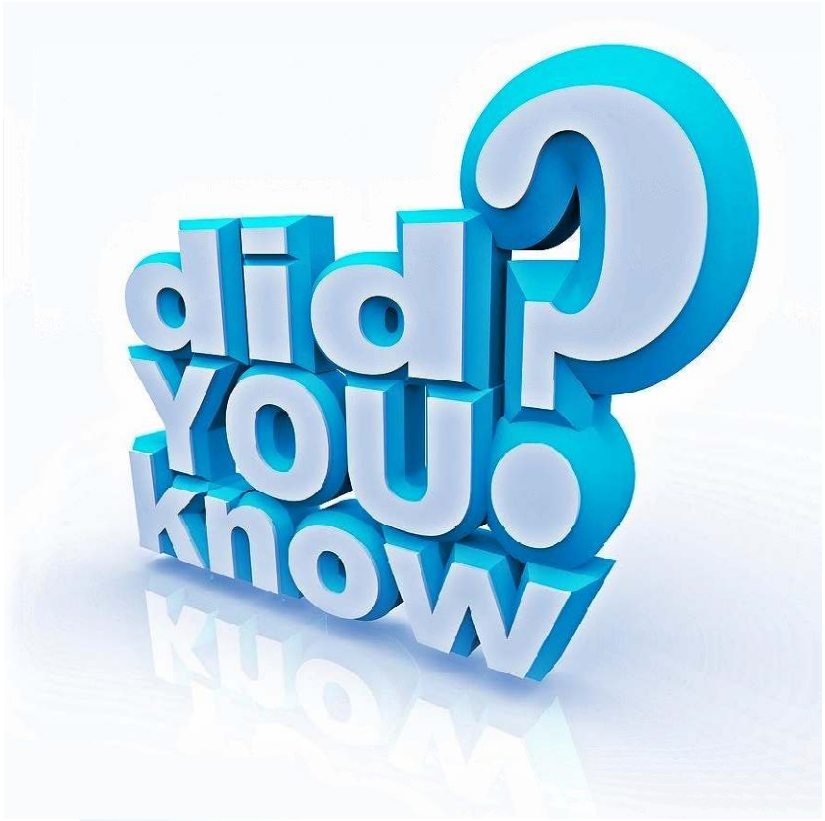
LIMITATIONS

- Patients with CKD were ***excluded from 75% of published coronary artery disease trials***
- Data are prinicipally based ***on observational non randomized trials, registries, cohorts or meta-analyses***
- ***Heterogeneous CKD population*** analyzed in many studies (pts on dialysis or severely impaired renal function are mixed with pts with moderate or mild renal dysfunction)
- Different acute kidney injury definitions

REVASCULARIZATION for Coronary artery disease in CKD or ESRD

Are patients with renal failure good candidates for percutaneous coronary revascularization?

REVASCULARIZATION for Coronary artery disease in CKD or ESRD



To dilate or not to dilate?

The literature has been very consistent in showing an increased risk of percutaneous coronary interventions in patients with chronic kidney disease

REVASCULARIZATION for Coronary artery disease in CKD or ESRD

CKD pts. have an unfavorable profile

✓ ***Older***

✓ ***Clinical syndromes known to be associated with periprocedural complications:***

- diabetes
- hypertension
- lower left ventricular ejection fraction
- chronic obstructive pulmonary disease
- vascular disease
- congestive heart failure
- cardiogenic shock
- multivessel disease
- history of prior CABG
- history of previous myocardial infarction

✓ ***Angiographic characteristics:***

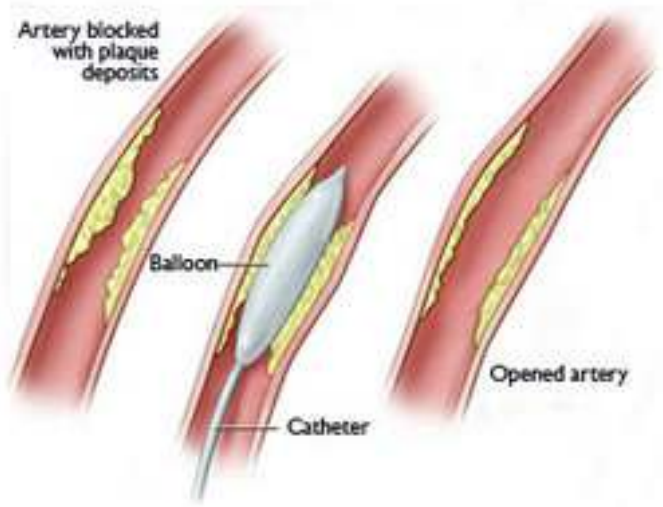
- small diffusely diseased vessels
- multivessel disease
- extensive intimal and medial coronary calcification

Rubenstein MH . Are patients with renal failure good candidates for percutaneous coronary revascularization in the new device era? Circulation. 2000;102:2966–2972.

REVASCULARIZATION for Coronary artery disease in CKD or ESRD

To dilate or not to dilate?

Many studies performed in the pre-stent era reported unfavourable outcomes with balloon angioplasty in CKD.



<u>High rates of procedural complications (up to 10%) and restenosis (up to 80%)</u> **meant that percutaneous coronary intervention (PCI) was thought to be ineffective in advanced renal disease**

<u>The introduction of coronary artery stenting appears to have improved both early success rates and long-term outcomes</u>

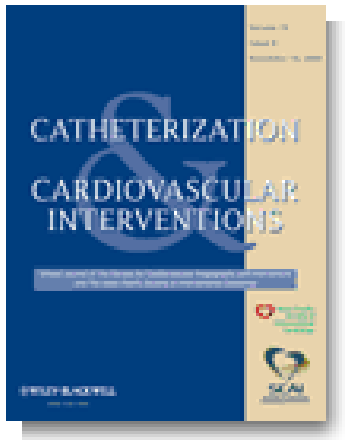
Treatment of coronary artery disease in hemodialysis patients: PTCA vs. stent

Robert M. Malanuk MD*, Christopher D. Nielsen MD, Paul Theis, Michael E. Assey MD, Bruce W. Usher MD and Robert B. Leman MD

Article first published online: 19 NOV 2001

DOI: 10.1002/ccd.1311

Issue



Catheterization and Cardiovascular Interventions

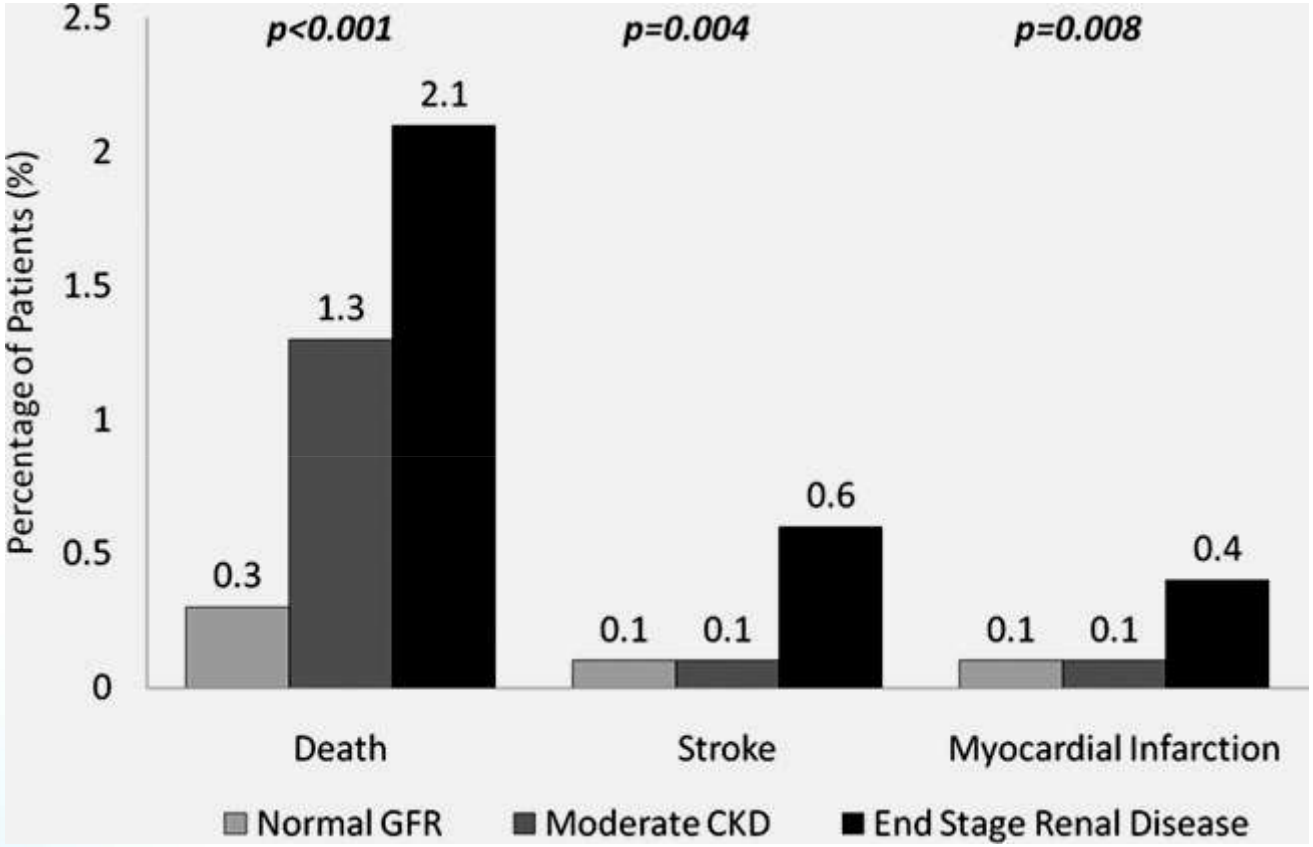
Volume 54, Issue 4, pages 459–463, December 2001

Intracoronary stent placement is both safe and feasible and produces more favorable clinical outcomes in the management of coronary disease in hemodialysis patients

Clear reduction in major cardiac events and mortality, from 71% to 30%, in patients in whom a stent was implanted

PCI IN CKD-IN HOSPITAL OUTCOME

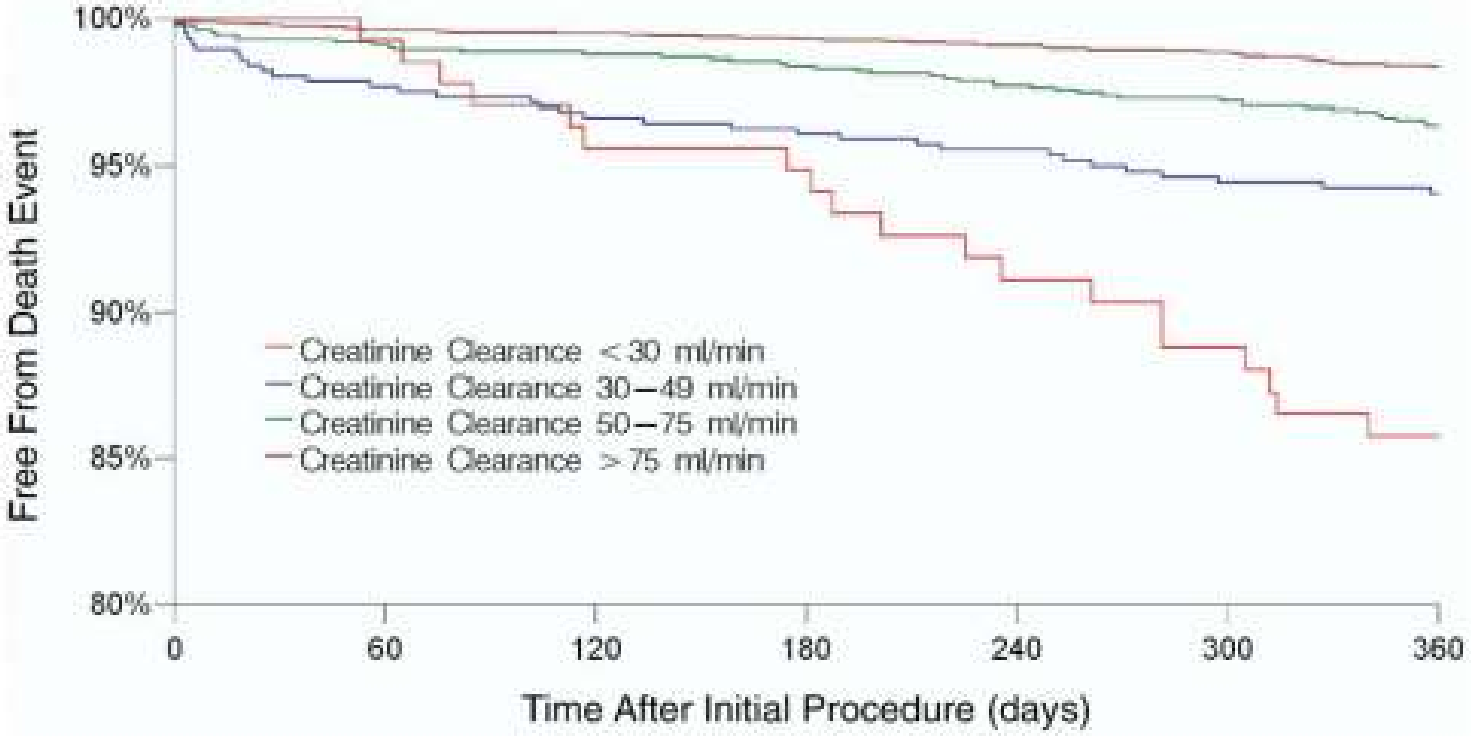
(ACS and DES implantation more frequent in pts with preserved GFR)



NY registry, 2004-2007
n=474 dialysis,
n= 6596 GFR<60,
n=17948 GFR>60

Parikh et al, CCI 2012

In-Hospital and 1-Year Outcomes Among Percutaneous Coronary Intervention Patients With Chronic Kidney Disease in the Era of Drug-Eluting Stents (J Am Coll Cardiol Intv 2009;2:37– 45)



With decreasing CrCl, there was a stepwise increase in mortality across all groups

In-Hospital and 1-Year Outcomes Among Percutaneous Coronary Intervention Patients With Chronic Kidney Disease in the Era of Drug-Eluting Stents (J Am Coll Cardiol Intv 2009;2:37– 45)

	Creatinine Clearance				
	>75 ml/min (n = 2,827)	50–75 ml/min (n = 1,253)	30–49 ml/min (n = 571)	<30 ml/min (n = 140)	p Value
In-hospital					
Death	0.1%	0.2%	0.9%	0.0%	0.0206
MI	5.7%	7.3%	8.2%	10.0%	0.0023
Death or MI	5.8%	7.4%	8.4%	10.0%	0.0016
Composite bleeding*	3.3%	5.0%	8.8%	14.3%	<0.0001
TIMI major	0.2%	0.3%	1.2%	0.0%	0.5587
TIMI minor	0.8%	1.3%	1.2%	0.0%	0.0567
Access site complications†	1.9%	2.9%	3.0%	0.7%	0.3121
Transfusion	1.6%	3.0%	6.3%	13.6%	<0.0001
Post-procedure length of stay (days), mean ± SD (n)	1.56 ± 2.37 (2,826)	1.63 ± 1.73 (1,253)	2.19 ± 2.73 (571)	2.49 ± 2.84 (140)	

During the index hospital stay, there was a step-wise increase in bleeding complications with decreasing CrCl (3.3%, 5.0%, 8.8%, and 14.3%; p< 0.0001 for trend)

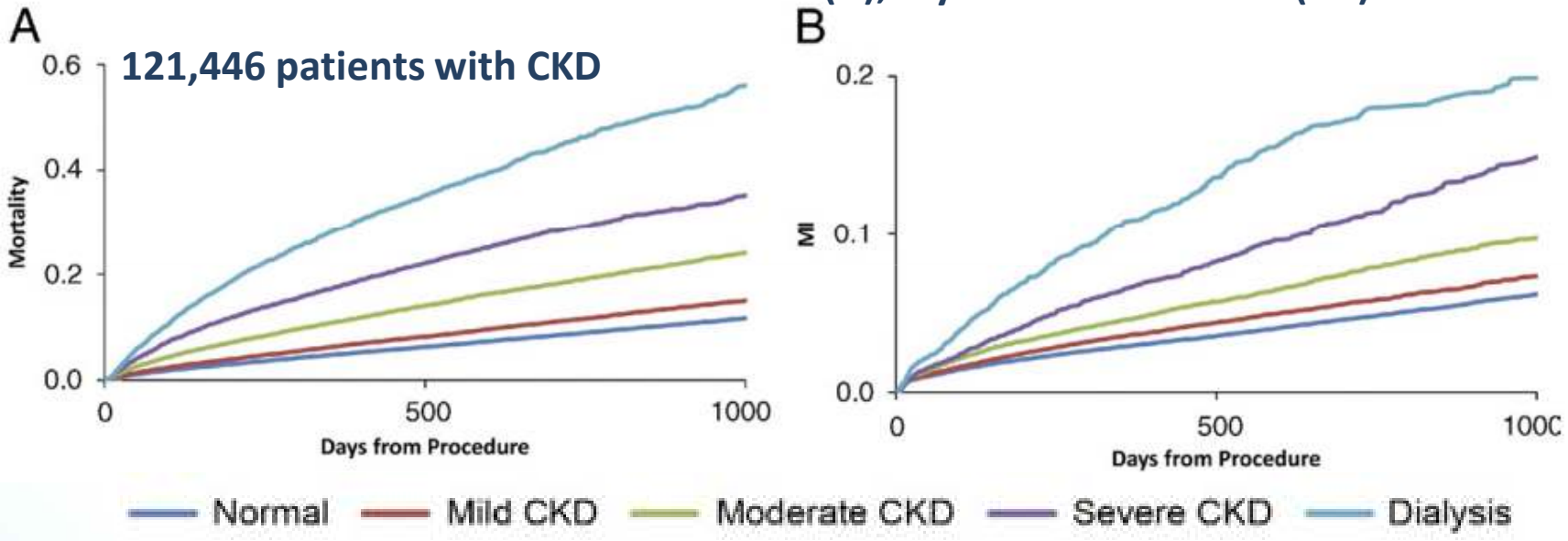
Safety and Efficacy of Drug-Eluting Stents in Older Patients With Chronic Kidney Disease

A Report From the Linked CathPCI Registry–CMS Claims Database

J Am Coll Cardiol. 2011; 58(18):1859-1869.

Increasing severity of CKD was associated with increasing rates of death and MI

Cumulative incidence for death (A), myocardial infarction (MI)



- **Mortality rates were extremely high in patients with severe CKD, with 30-month mortality rates of 32.7% and peaked in patients on long-term dialysis at 51.9%**
- **Dialysis patients also had the highest adjusted rates of MI**

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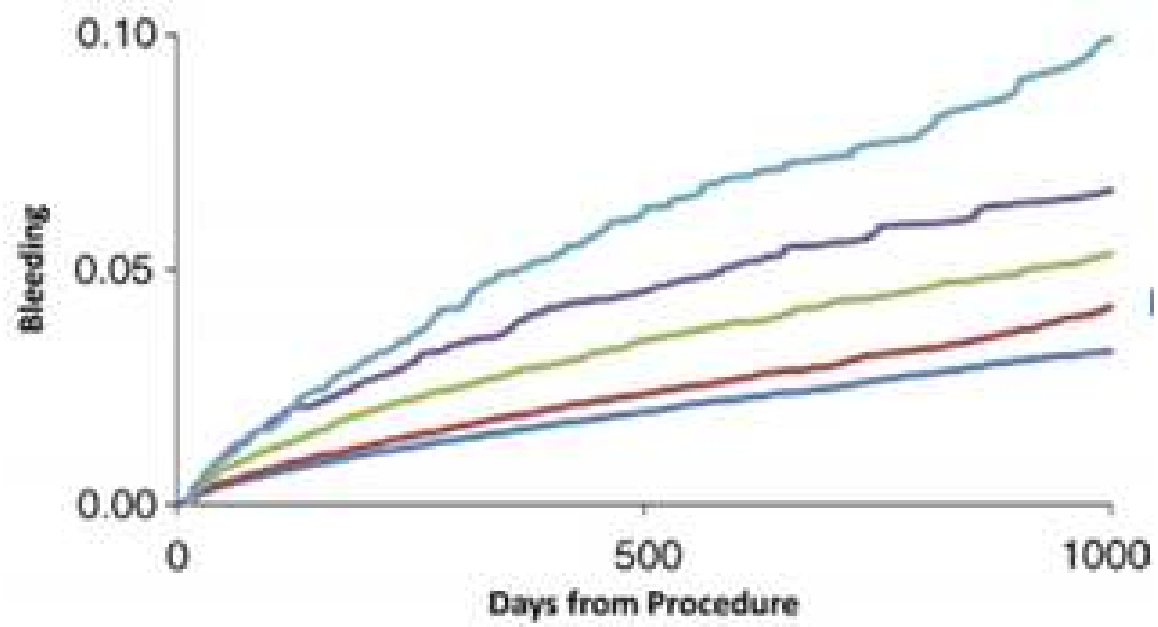
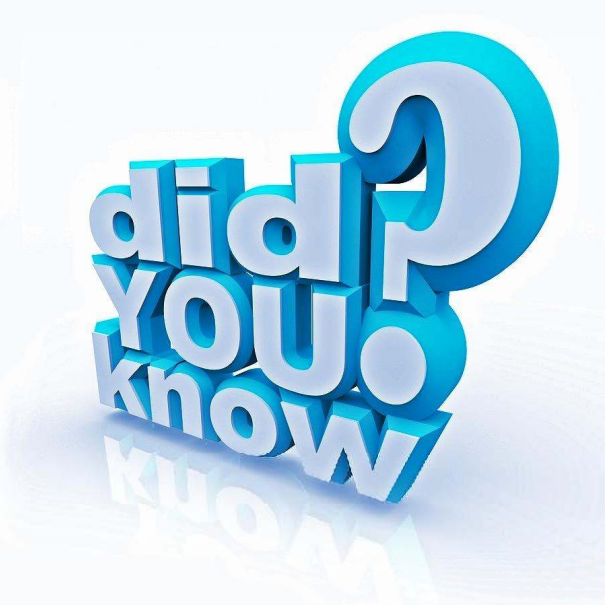
Increasing severity of CKD was also associated with increasing rates of major bleeding



121,446 patients with CKD (GFR< 60 ml/min/1.73 m2).

Dialysis patients had the highest adjusted rates of major bleeding (adjusted HR: 2.27; 95% CI: 1.97 to 2.60)

CKD and PCI: Reasons for higher bleeding rates



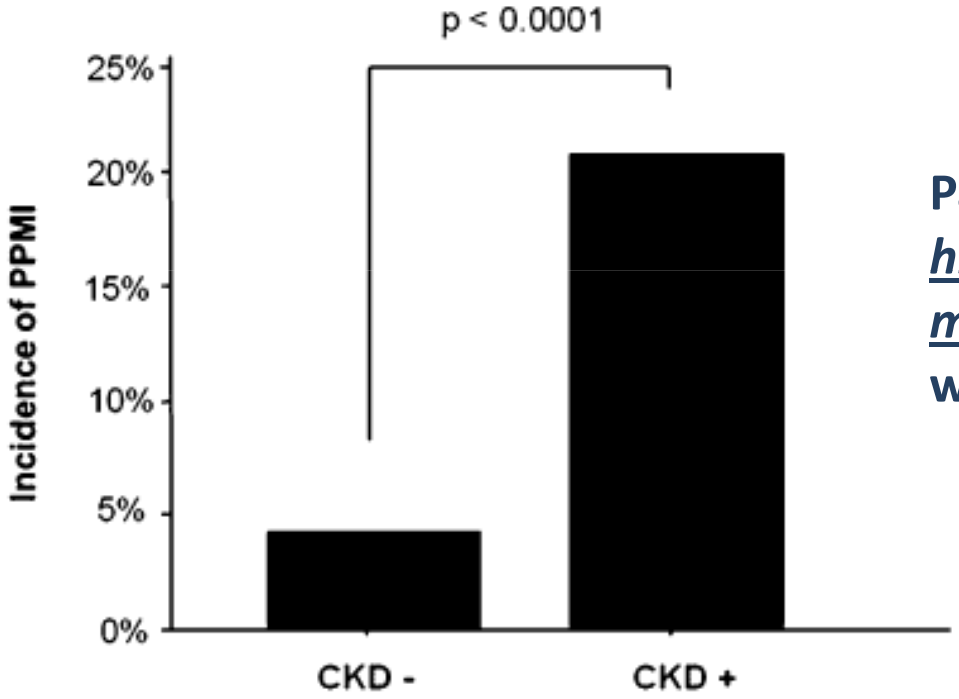
Inappropriately high doses of antithrombotic agents (especially heparine and IIb-IIIa inhibitors) due to an underestimation of the severity of CKD on the basis of serum creatinine

Alexander et al, CIRCULATION 2006

Impact of chronic kidney disease on the incidence of peri-procedural myocardial injury in patients undergoing elective stent implantation

Soichiro Kumagai[1,2] Hideki Ishii[1], Tetsuya Amano[1,2], Tadayuki Uetani[2], Bunichi Kato[2], Ken Harada[1,2], Tomohiro Yoshida[1,2], Hirohiko Ando[1,2], Ayako Kunimura[1,2], Yusaku Shimbo[1,2], Katsuhide Kitagawa[1,2], Kazuhiro Harada[1,2], Mutsuharu Hayashi[1], Daiji Yoshikawa[1], Tatsuaki Matsubara[3] and Toyoaki Murohara[1]

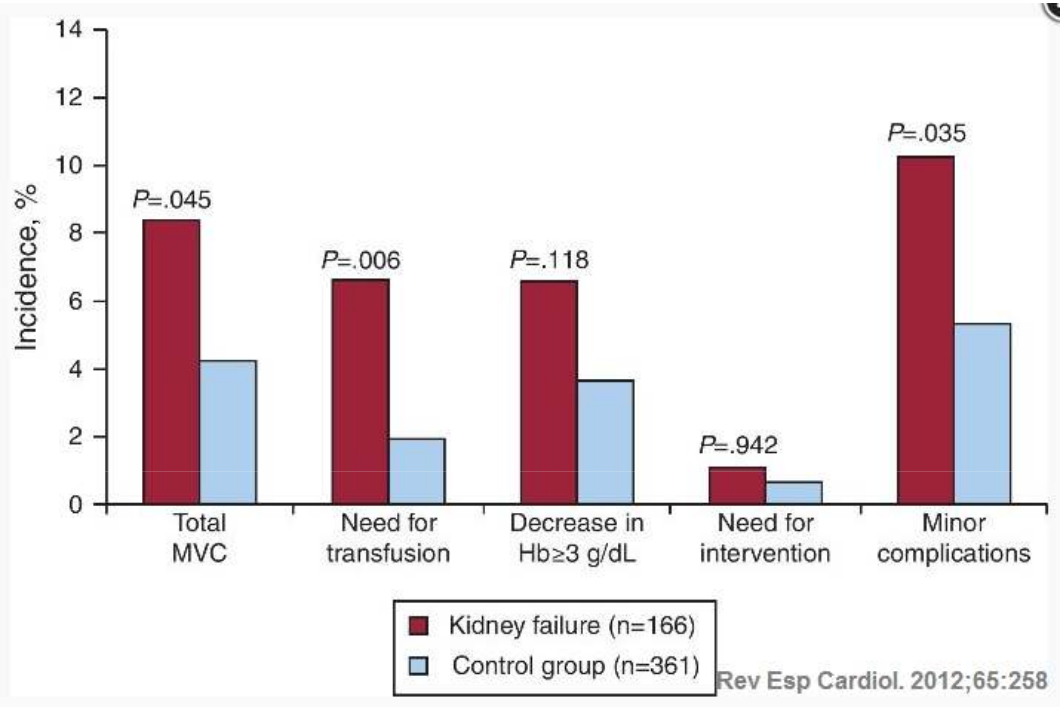
Nephrol Dial Transplant (2012) 27: 1059–1063



Patients with CKD had *a significantly higher incidence of peri-procedural myocardial injury* compared to those without (4.3 versus 20.9%, P < 0.0001).

Renal Insufficiency and Vascular Complications After Primary Angioplasty Via Femoral Route. Impact of Vascular Closure Devices Use

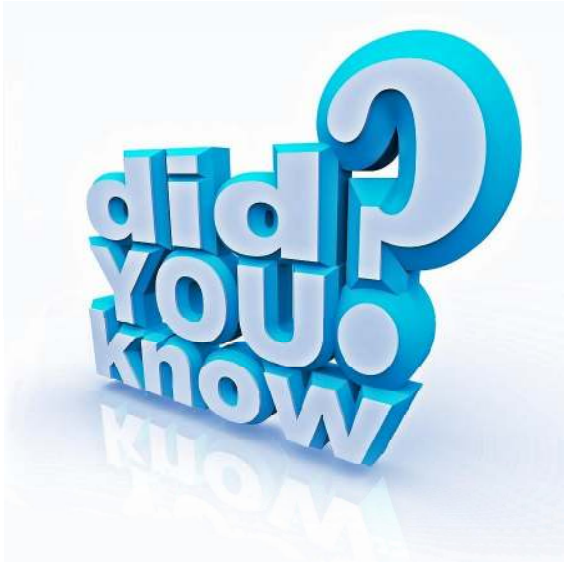
REVISTA ESPAÑOLA DE CARDIOLOGIA



Patients with chronic kidney disease undergoing primary angioplasty via the femoral route <u>experience higher rates of major vascular complications.</u>

Patients with CKD and especially ESRD have higher in-stent restenosis rates with both bare-metal and drug eluting stents

This has been attributed to:



- **higher incidences of DM,**
- **higher incidences diffuse atherosclerosis,**
- **higher incidences calcifications**
- **enhanced oxidative stress and granulocyte activation**

BMS vs DES in patients with CKD

There is limited data and often conflicting results regarding the safety and efficacy of DES compared to BMS in patients with renal dysfunction

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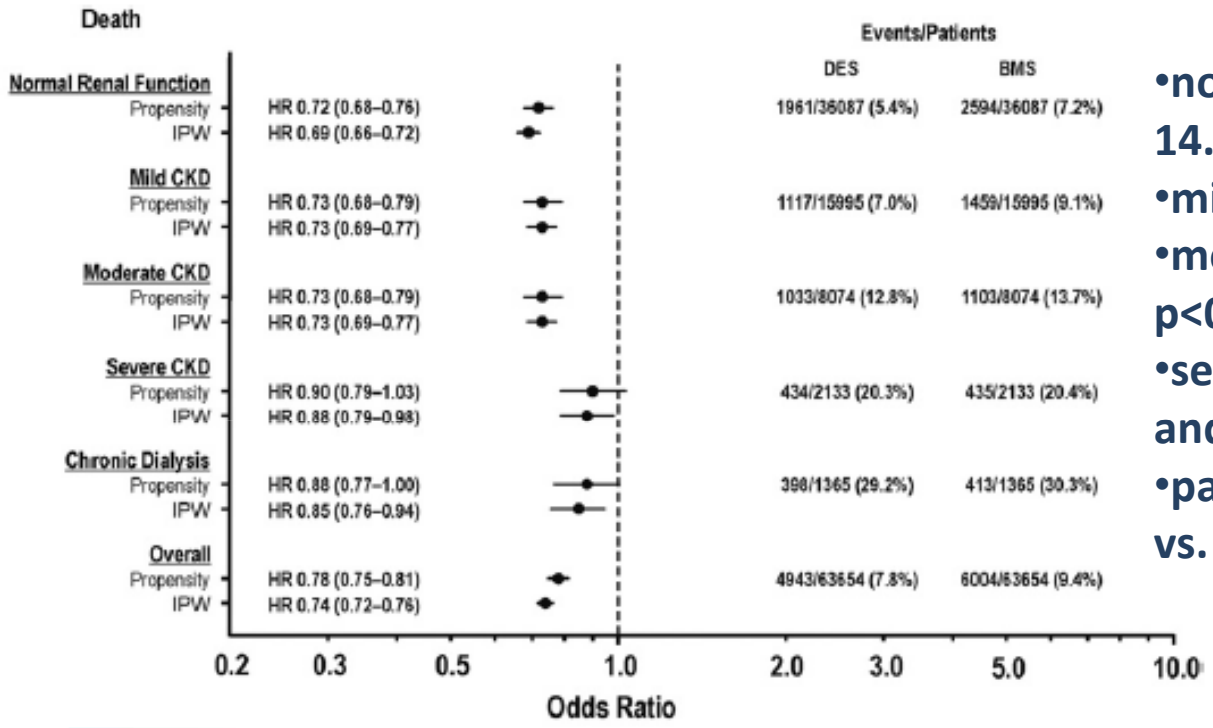

- **normal renal function (12.2% vs. 14.7%, p < 0.001),**
- **mild CKD (15.1% vs. 18.6%, p<0.001)**
- **moderate CKD (24.1% vs. 26.6%, p<0.001)**
- **severe CKD (33.7% vs. 33.7%, p<0.04) and**
- **patients on long-term dialysis (48.9% vs. 56.4%, p <0.001)**

Compared with BMS, DES treatment was associated with lower 30-month death rates

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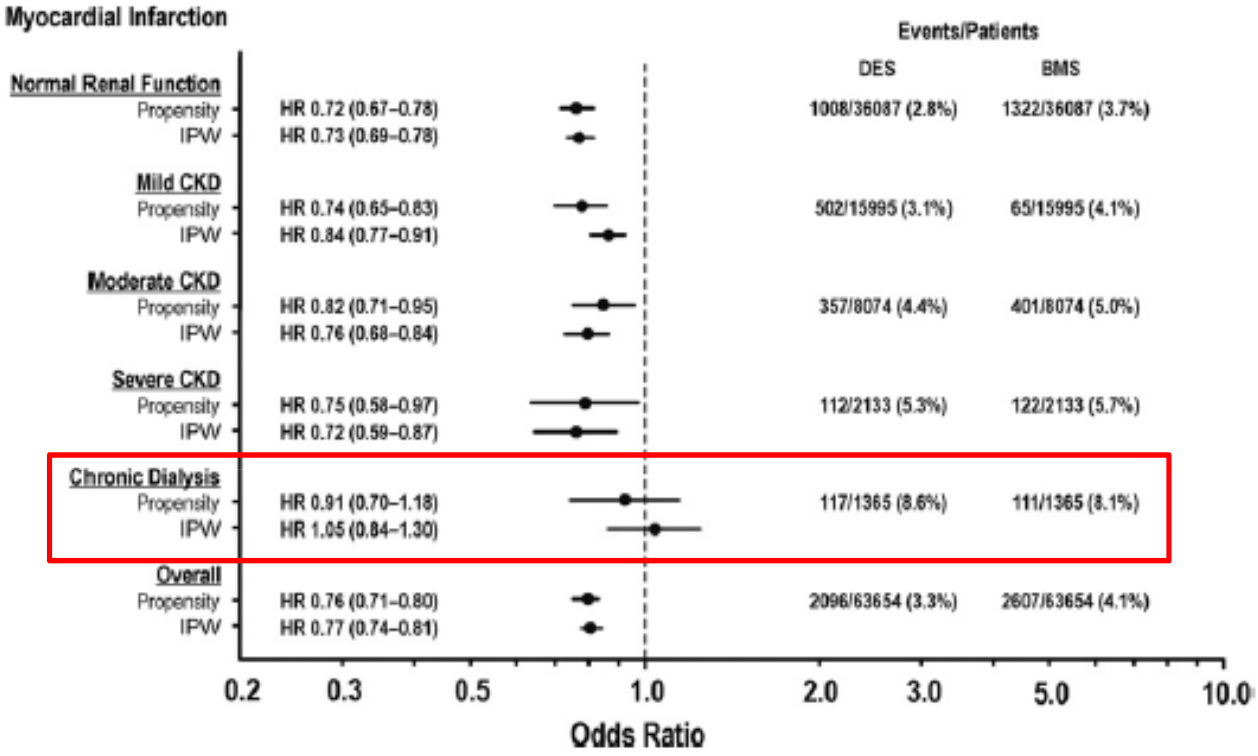


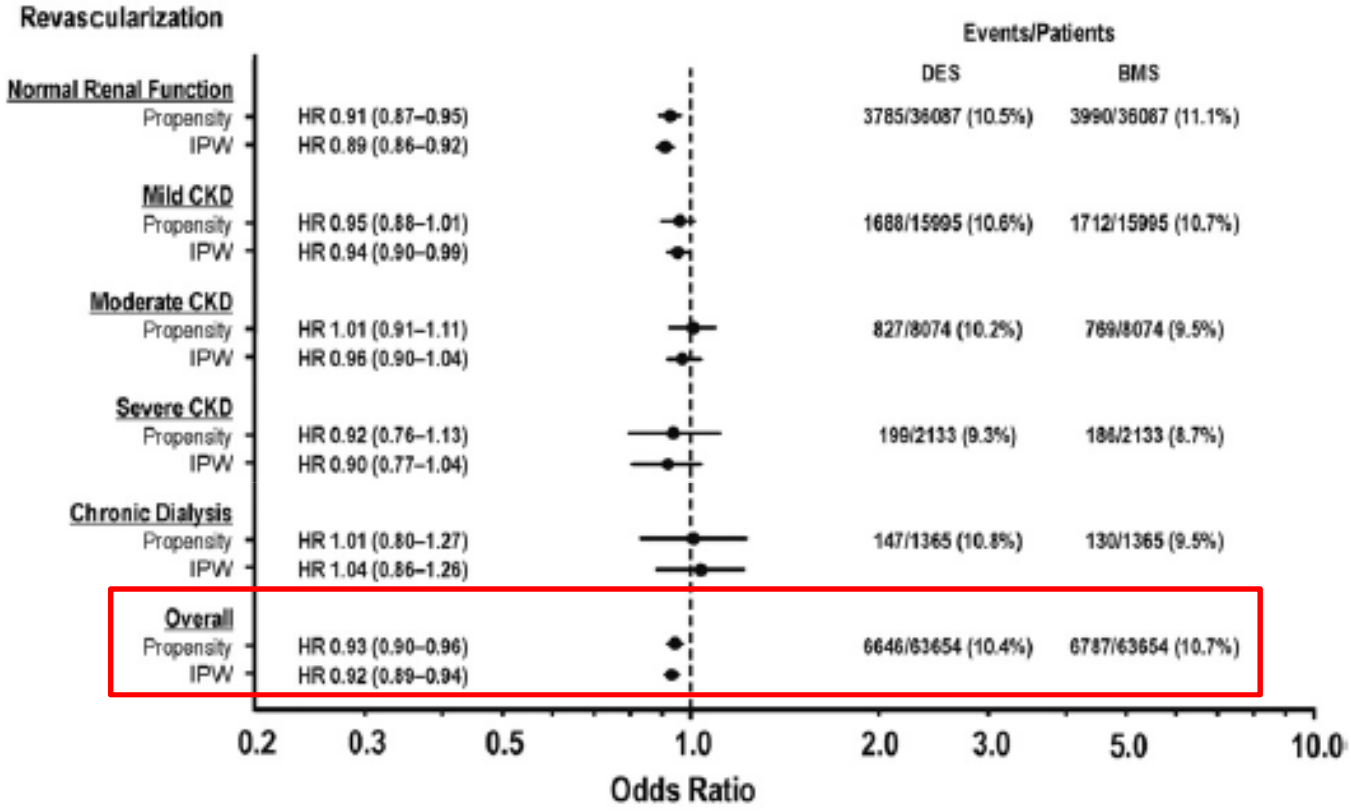
This pattern was not observed in patients on long-term dialysis.

The use of DES compared with BMS was also associated with lower adjusted 30-month MI rates in patients with normal renal function or mild, moderate, or severe CKD.

Safety and Efficacy of Drug-Eluting Stents in Older Patients With Chronic Kidney Disease

A Report From the Linked CathPCI Registry–CMS Claims Database

J Am Coll Cardiol. 2011; 58(18):1859-1869.



Patients with mild, moderate, or severe CKD and patients on dialysis did not show significant differences in revascularization rates for DES compared with BMS .

Comparison of Bare-Metal and Drug-Eluting Stents in Patients with Chronic Kidney Disease (from the NHLBI Dynamic Registry)

Am J Cardiol. 2011 December 1; 108(11): 1658–1664

The American Journal of Cardiology

The effect of DES in reducing repeat revascularization appeared to be attenuated in these patients.

Event	Low Glomerular Filtration Rate		
1-year adverse outcomes	BMS (n=345)	DES (n=763)	p-value
Death	8.0%	5.8%	0.16
MI	6.9%	5.1%	0.27
Death/MI	13.8%	10.2%	0.08
Repeat PCI	10.2%	8.7%	0.39
Repeat Revascularization	12.2%	9.9%	0.23
MACE	21.6%	16.6%	0.051

DES use in this patient population did not appear to be associated with an increased hazard of death or MI when compared to BMS.

Given the trends observed, however, one cannot discount the possibility that with a larger sample size, a beneficial effect could be seen.

Drug-Eluting Stents Versus Bare-Metal Stents in Patients With Decreased GFR: A Meta-analysis

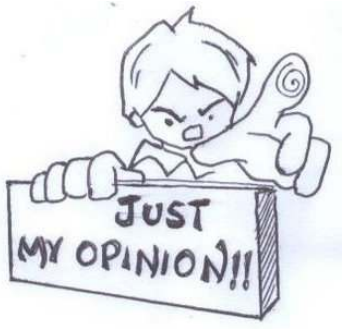
Am J Kidney Dis. 2013 Oct;62(4):711-21.

Data from 26 comparative studies ***with 66,840 patients*** were included.

Compared with BMSs, DESs were associated with significant reductions in:

- repeat revascularization (OR, 0.61; 95% CI, 0.50-0.74; *P* < 0.001) and
- myocardial infarction (OR, 0.85; 95% CI, 0.79-0.92; *P* < 0.001),
- mortality also was documented (OR, 0.77; 95% CI, 0.65-0.90; *P* = 0.01).
- with no detectable difference in stent thrombosis (OR, 0.72; 95% CI, 0.46-1.12; *P* = 0.1).

These data support the use of DES in patients with CKD



✓**In summary, the use of stents *and particularly drug eluting stents has decreased the rates of in-stent restenosis, but these rates remain higher than in patients with normal renal function.***

✓***There does not appear to be any signal of harm in any CKD subgroup including dialysis patients.***

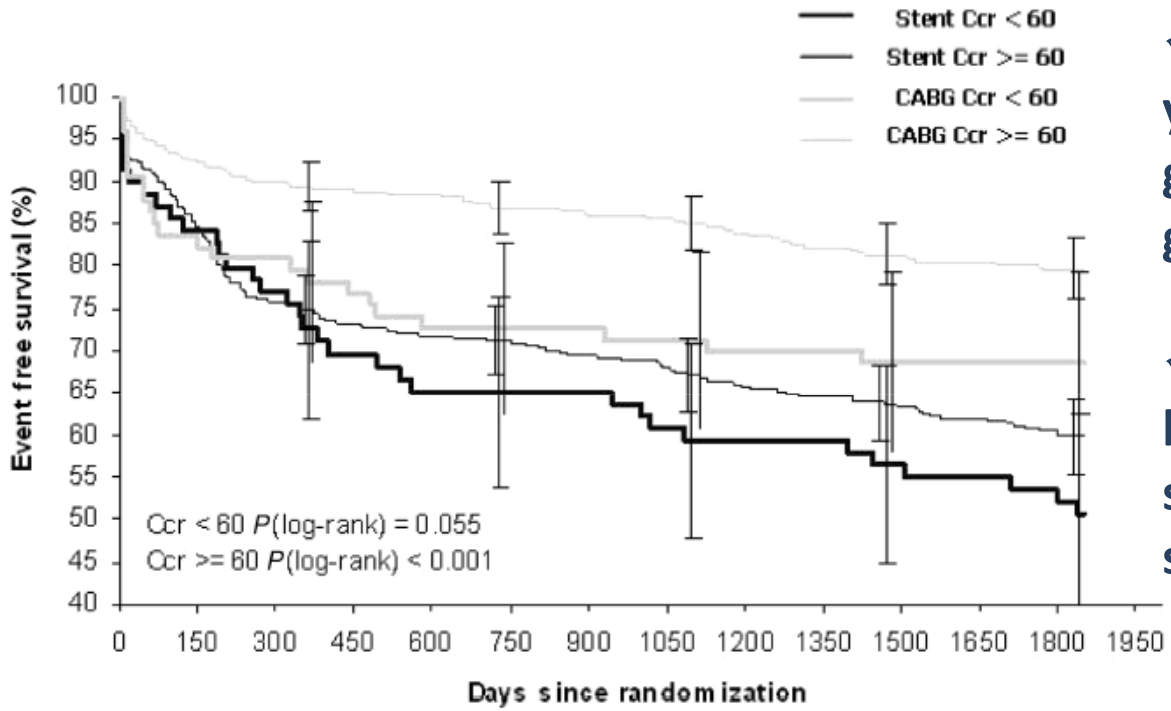
For now, the clinical treatment of CKD patients undergoing PCI should be focused *on adequate stent deployment with judicious use* of antiplatelet and antithrombotic management


CABG
PCI

Five year clinical effect of coronary stenting and coronary artery bypass grafting in renal insufficient patients with multivessel coronary artery disease: insights from ARTS trial

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal (2005) 26, 1488–1493



✓**The event-free survival at 5 years was 50.7% in the stent group and 68.5% in the surgery group (P< 0.04)**

✓**The differences in mortality between coronary stenting and surgery did not reach statistically significant level.**

The occurrence of MACCE in the stent group was higher than in the CABG group, *mainly driven by the higher incidence of repeat revascularization in the stent group.*

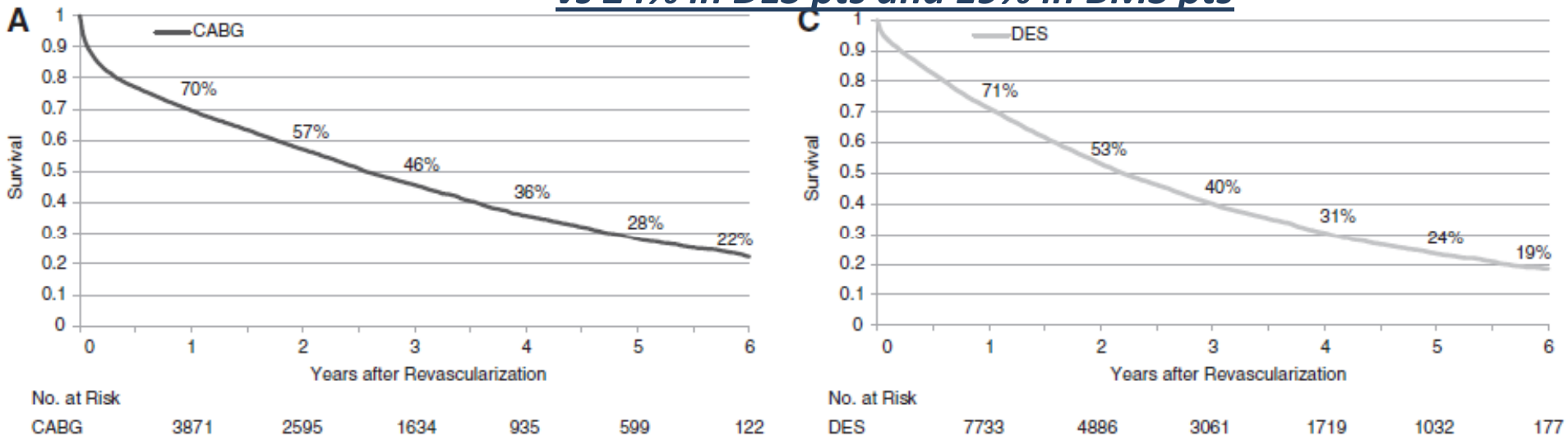
Long-Term Survival and Repeat Coronary Revascularization in Dialysis Patients After Surgical and Percutaneous Coronary Revascularization With Drug-Eluting and Bare Metal Stents in the United States

Gautam R. Shroff, Craig A. Solid and Charles A. Herzog

Circulation. 2013;127:1861-1869

23033 dialysis patients who underwent coronary revascularization

Long-term survival (5 years) was superior with CABG 28%, vs 24% in DES pts and 19% in BMS pts



In-hospital mortality was significantly higher in CABG pts

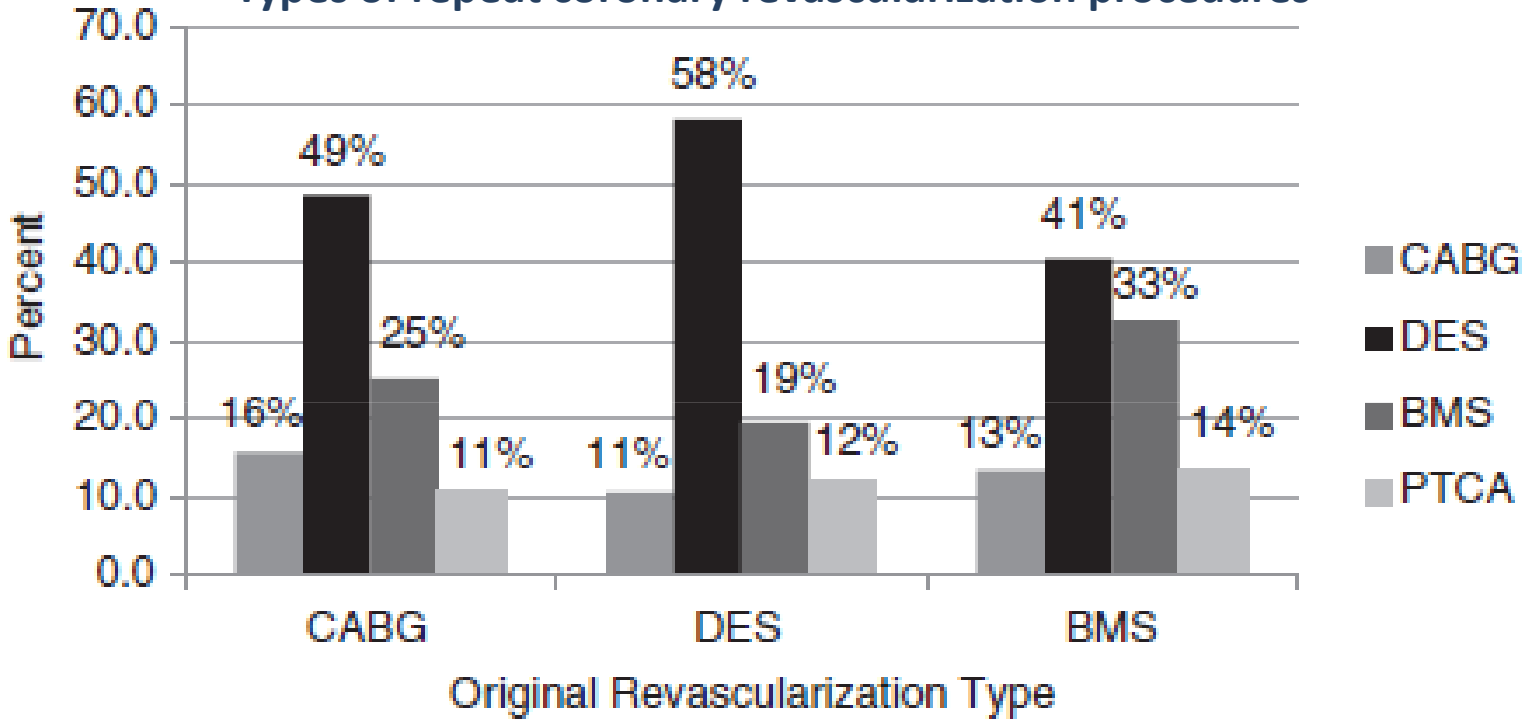
- **CABG 8.2%**
- **DES 2.7%**
- **BMS 4.9%**

Long-Term Survival and Repeat Coronary Revascularization in Dialysis Patients After Surgical and Percutaneous Coronary Revascularization With Drug-Eluting and Bare Metal Stents in the United States

Gautam R. Shroff, Craig A. Solid and Charles A. Herzog

Circulation. 2013;127:1861-1869

Types of repeat coronary revascularization procedures



The probability of repeat revascularization was 18% with bare metal stents, 19% with DES, and 6% with coronary artery bypass grafting at 1 year.

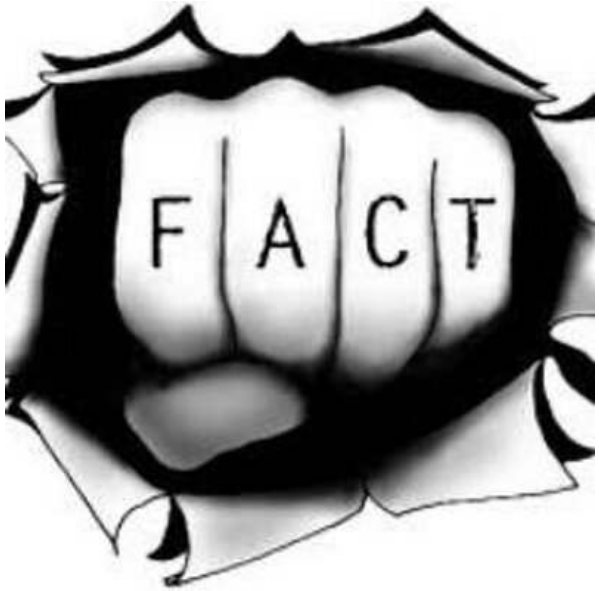
Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the Europea Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) European Heart Journal (2010) 31, 2501–2555

Table 18 Specific recommendations for patients with mild to moderate chronic kidney disease

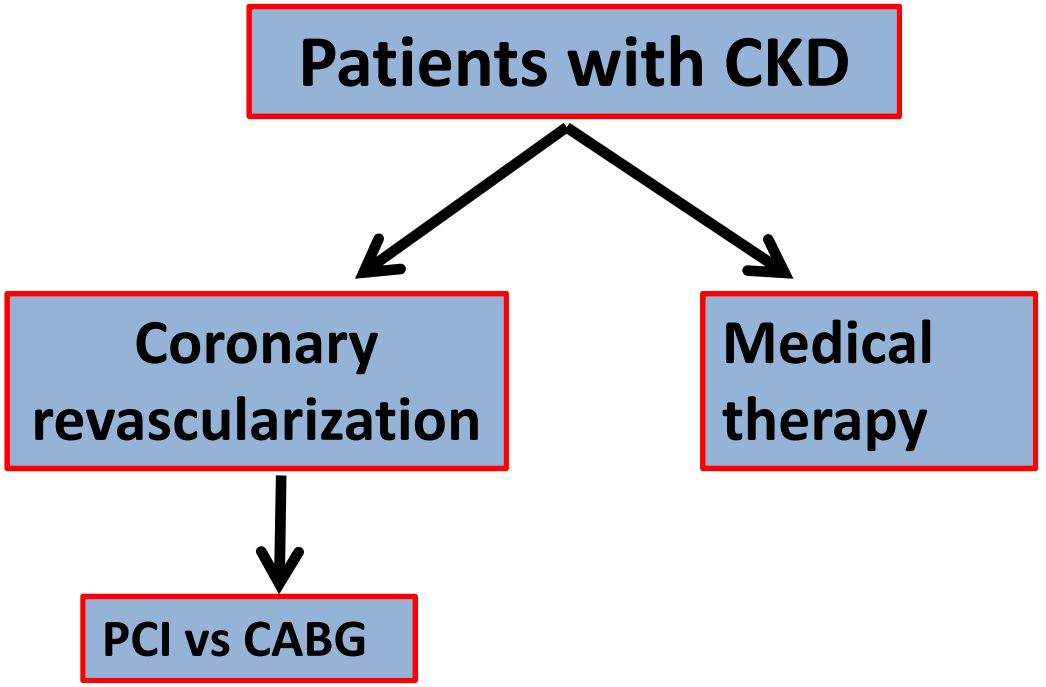
	Class[a]	Level[b]	Ref.[c]
CABG should be considered, rather than PCI, when the extent of the CAD justifies a surgical approach, the patient's risk profile is acceptable, and life expectancy is reasonable.	IIa	B	32, 137–139
Off-pump CABG may be considered, rather than on-pump CABG.	IIb	B	140
For PCI, DES may be considered, rather than BMS.	IIb	C	—

Revascularization in Patients With CKD



Revascularisation of coronary arteries with CABG and PCI is associated with greater mortality in patients with CKD and those on dialysis compared to the general population.

The more pertinent question is whether patients with CKD undergoing revascularization do better or worse than those treated with medical therapy alone.

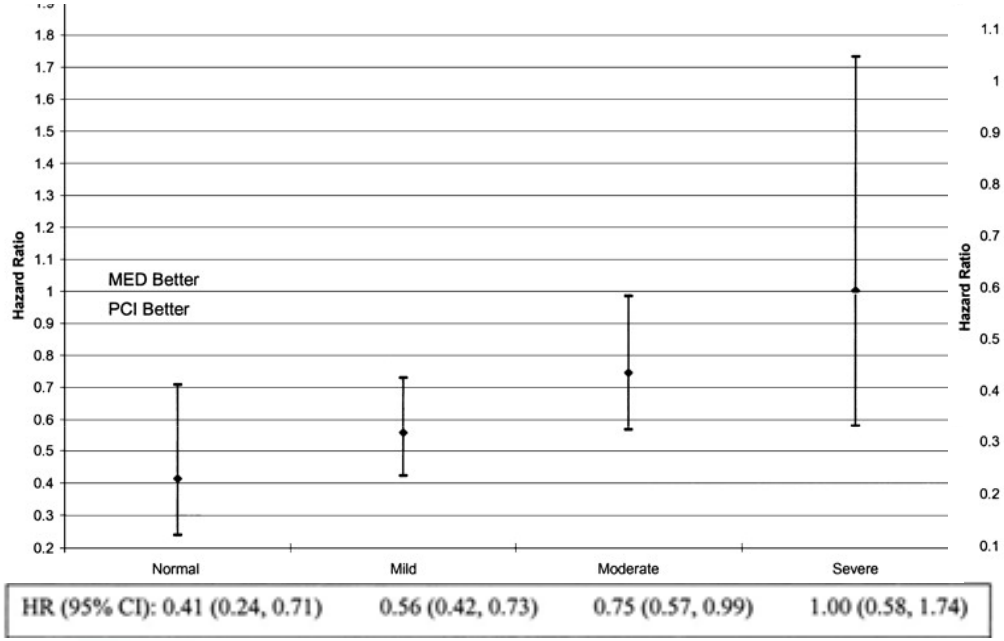


The data supporting the use of percutaneous coronary interventions over medical therapy in patients with chronic kidney disease is extremely limited and fraught with confounding data in the absence of a RCT

Chronic Kidney Disease, Mortality, and Treatment Strategies among Patients with Clinically Significant Coronary Artery Disease

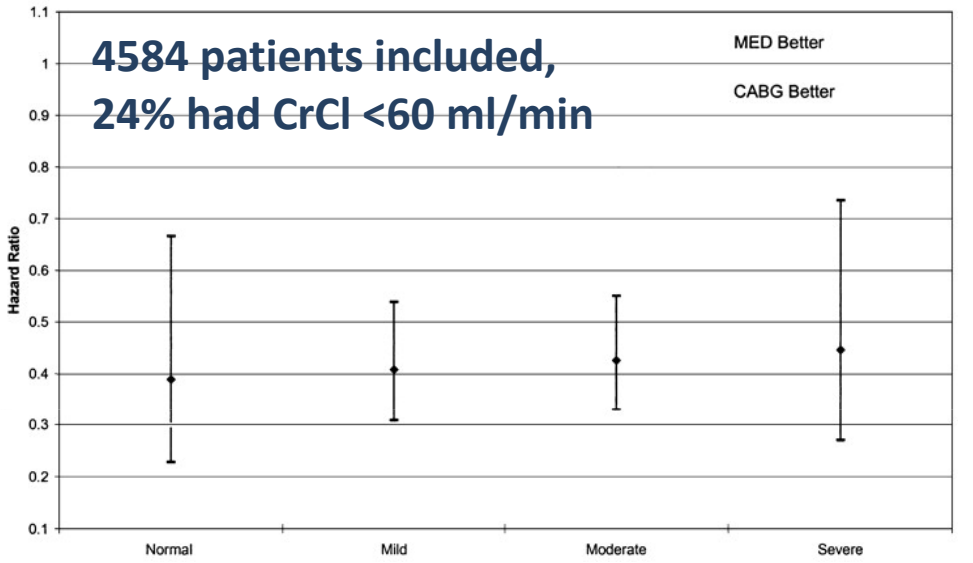
JASN

J Am Soc Nephrol. 2003 Sep;14(9):2373-80



HR (95% CI): 0.41 (0.24, 0.71)	0.56 (0.42, 0.73)	0.75 (0.57, 0.99)	1.00 (0.58, 1.74)

4584 patients included,
24% had CrCl <60 ml/min



HR (95% CI):0.39 (0.23, 0.66)	0.41 (0.31, 0.54)	0.43 (0.33, 0.55)	0.45 (0.27, 0.74)

PCI was associated with a survival benefit compared with medical management among patients with mildly, and moderately impaired renal function but not among patients with severe CKD

CABG was associated with a survival benefit among patients with with CKD compared with medical management.

Revascularization decisions for CKD patients should be individualized (adopt a heart team approach)

The decision to proceed with a conservative strategy with medical therapy versus a more aggressive strategy incorporating coronary revascularization requires consideration:

- **of the patient's symptoms,**
- **the amount of myocardium at risk,**
- **the presence and severity of impaired left ventricular function (reduced ejection fraction), and**
- **the severity of coronary artery disease.**

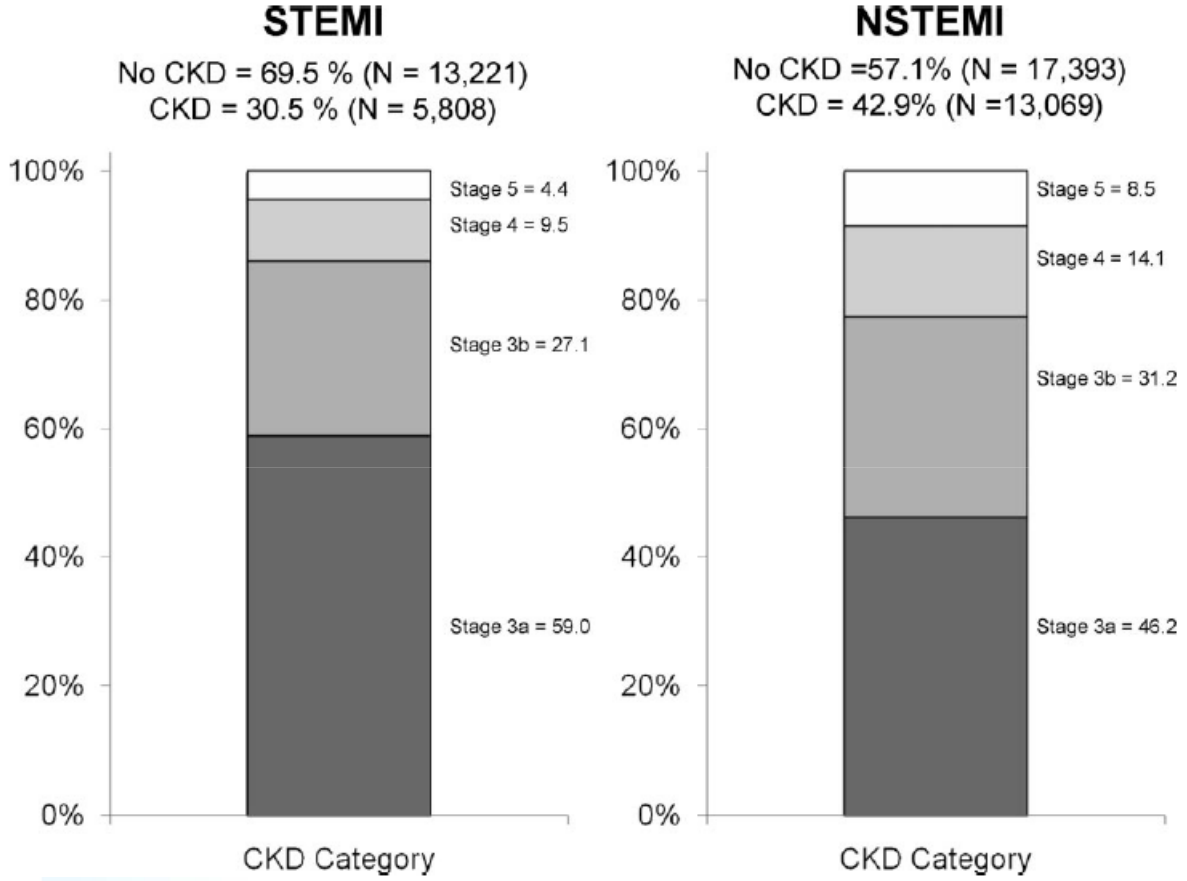
✓**We recommend that in patients with chronic kidney disease (CKD), end-stage renal failure (ESRF) and after kidney transplantation, that guidelines for revascularization of the general population be adhered to.**

✓**PCI may be a reasonable consideration in CKD patients in whom CABG is not an appropriate option in the revascularization strategy because of the higher perioperative mortality and morbidity or whose overall life expectancy is judged to be limited.**

ACUTE CORONARY SYNDROMES IN CKD

Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease

Circulation



Overall, nearly one third of patients presenting with STEMI and *>40% of patients presenting with NSTEMI*

Fox et al. Circulation. 2010;121:357-365

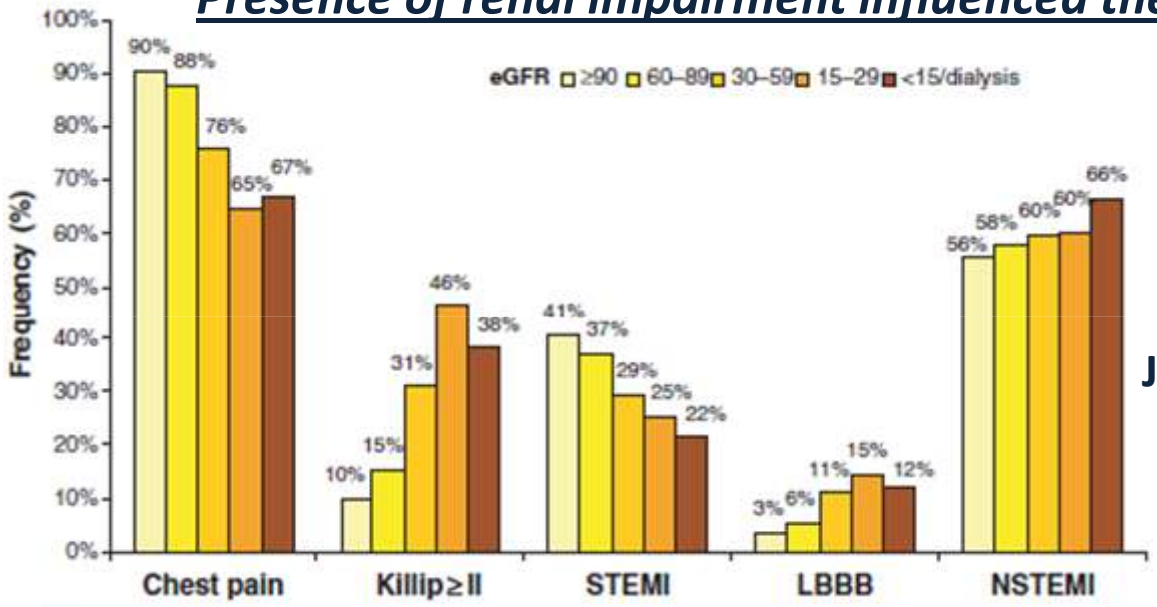
Original Article | Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2009.02204.x

Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: data from the SWEDEHEART register

K. Szummer[1], P. Lundman[2], S. H. Jacobson[3], S. Schön[4], J. Lindbäck[5], U. Stenestrand[6], L. Wallentin[5] & T. Jernberg[1], for SWEDEHEART

Presence of renal impairment influenced the clinical presentation for MI.

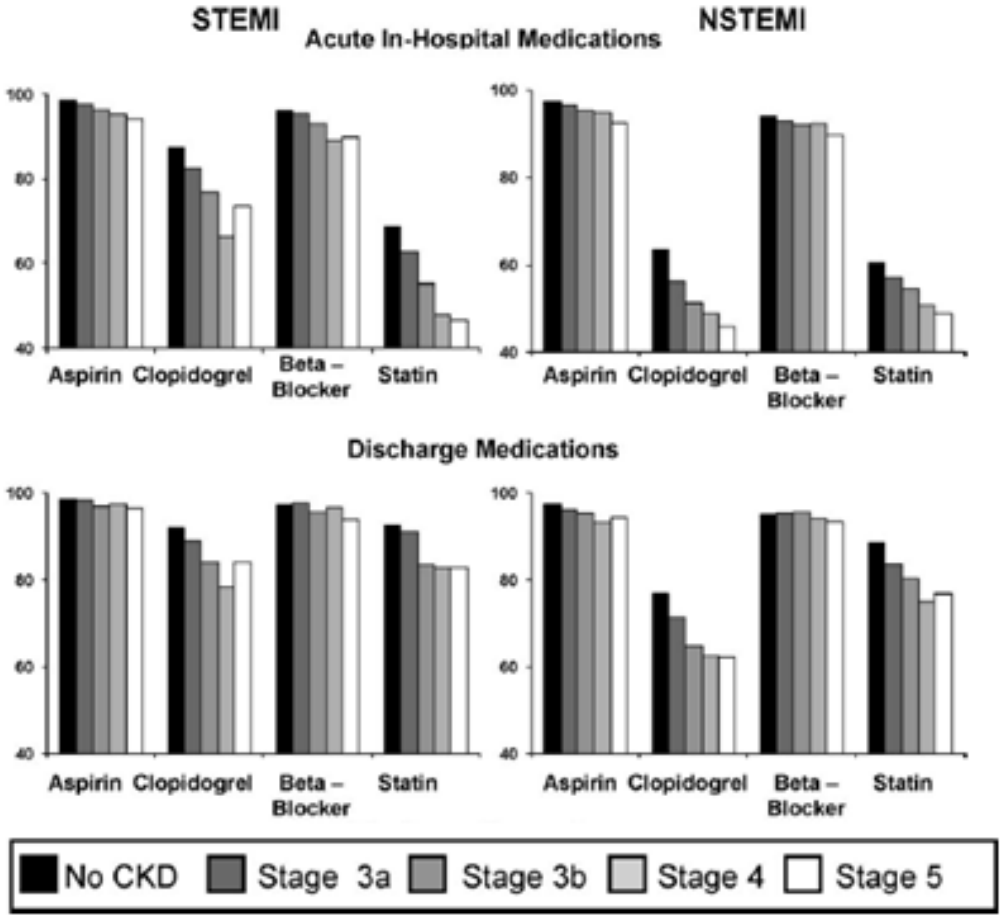


J InternMed2010;268:40–49.

More patients had heart failure and fewer presented with typical symptoms and ECG.
Lack of chest pain and pre-existing left bundle branch block results in a lower suspicion of MI, and likely contributes to a worse outcome

Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease

Circulation



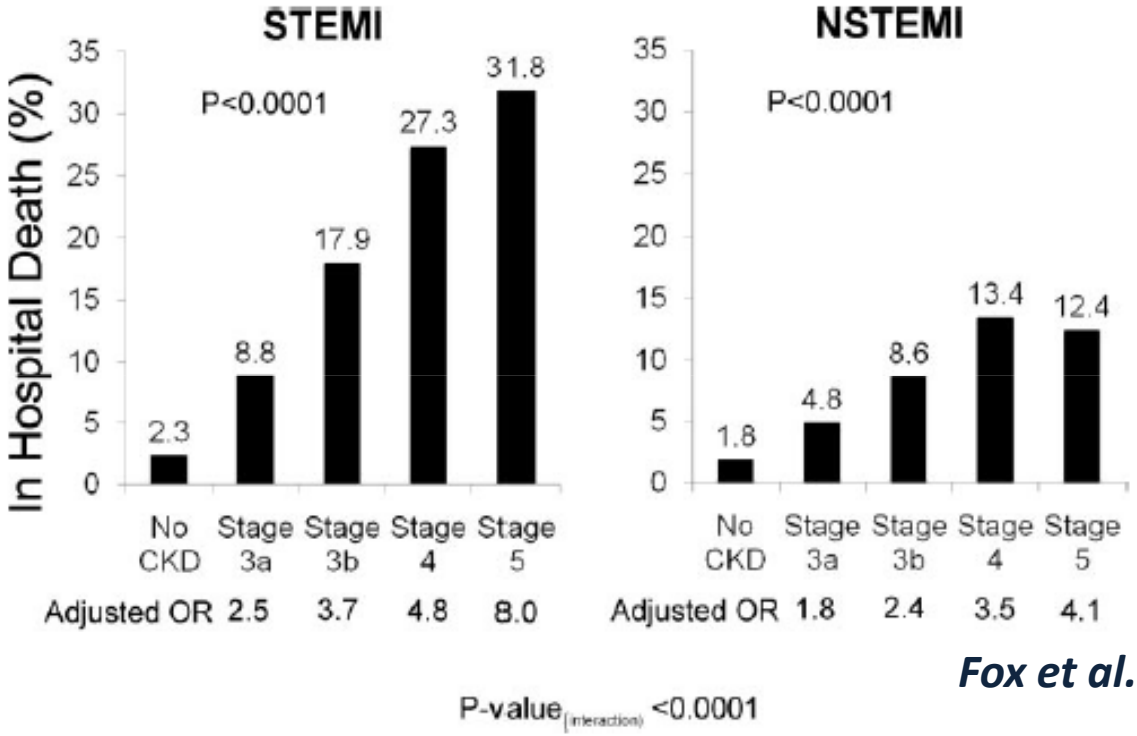
The present study also documented lower use of short-term therapies, in-hospital procedures, cardioprotective medications, and higher rates of medication overdosing among patients with CKD.

Fox et al. Circulation. 2010;121:357-365

Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Overall, the risk of mortality increased with CKD stage



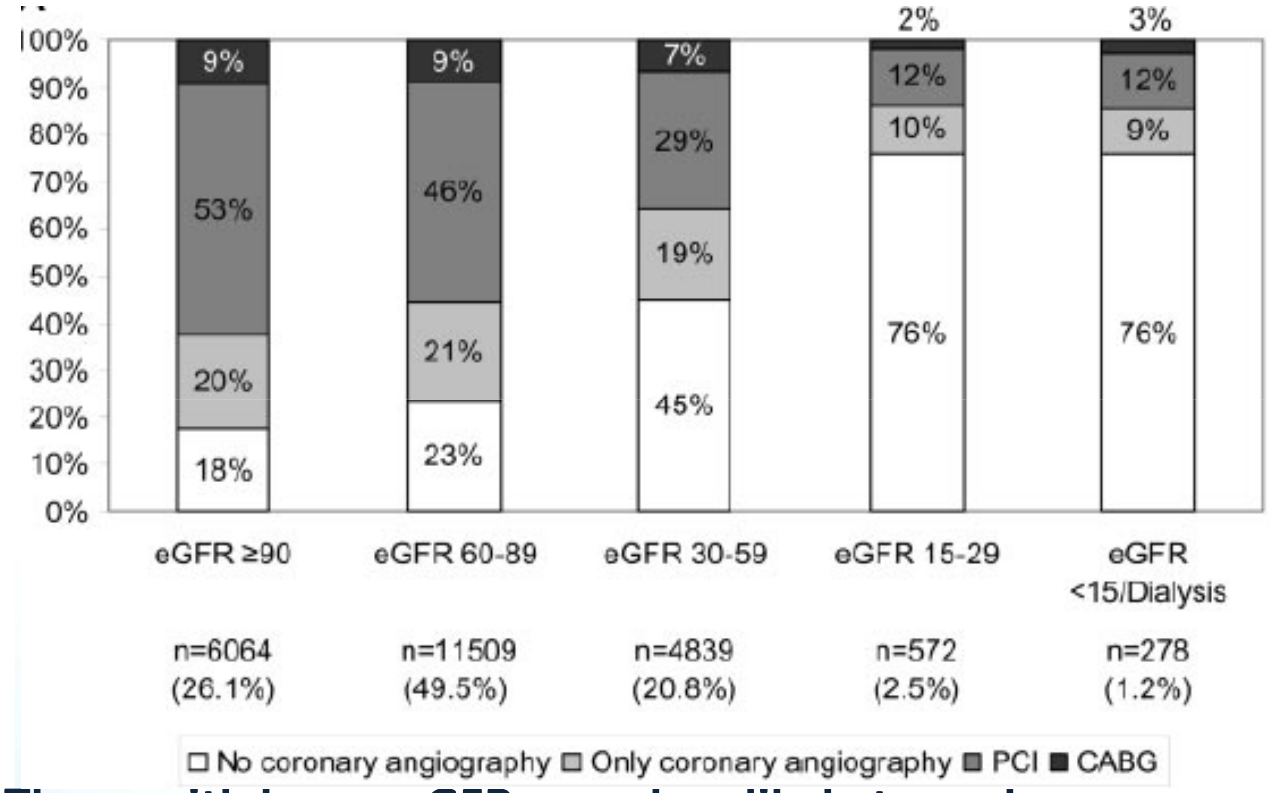
Odds ratios for death being 4 to 8 times higher among those with stage 5 CKD than among patients without CKD

Fox et al. Circulation. 2010;121:357-365.)

However, there was a greater relative increase in death for patients with STEMI with advancing CKD stage than was seen in NSTEMI

Influence of Renal Function on the Effects of Early Revascularization in Non-ST-Elevation Myocardial Infarction: Data From the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART)

Circulation



A total of 23262

consecutive non–ST-elevation myocardial infarction patients <80 years old

Szummer et al Circulation. 2009;120:851-858

Those with lower eGFR were less likely to undergo coronary angiography and to be revascularized within 14 days of admission

Temporal management patterns and outcomes of non-ST elevation acute coronary syndromes in patients with kidney dysfunction

Jorge A. Wong[1,2], Shaun G. Goodman[1,2], Raymond T. Yan[1,2], Ron Wald[3], Alan J. Bagnall[1,2], Robert C. Welsh[4], Graham C. Wong[5], Jan Korndер[6], Kim A. Eagle[7], Philippe Gabriel Steg[8], and Andrew T. Yan[1,2]* on behalf of the Canadian Acute Coronary Syndromes I and II, and Canadian Global Registry of Acute Coronary Events (GRACE/GRACE[2]) Investigators

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal (2009) 30, 549–557

	eGFR ≥60 mL/min/ 1.73 m² (*n* = 334)	eGFR <60 mL/min/ 1.73 m² (*n* = 345)	*P*-value
Patient not high risk (%)	46.7	37.7	0.02
Not supported by evidence (%)	6.3	7.8	0.46
Not high enough risk or not supported by evidence (%)	52.7	45.2	0.055
Renal insufficiency (%)	0.3	3.8	0.002
Significant comorbidity (%)	4.5	12.5	<0.001
Patient/family refused (%)	5.1	8.1	0.12
Previously defined anatomy unsuitable (%)	14.4	11.9	0.36
Previously defined anatomy and revascularization already planned (%)	7.5	3.8	0.044
Bleeding or other safety concerns (%)	1.5	7.2	<0.001
No reason given (%)	15.9	13.0	0.33
GRACE score of patients who were not considered high risk and did not undergo angiography[a]	110 (88–134)	140 (119–163)	<0.001

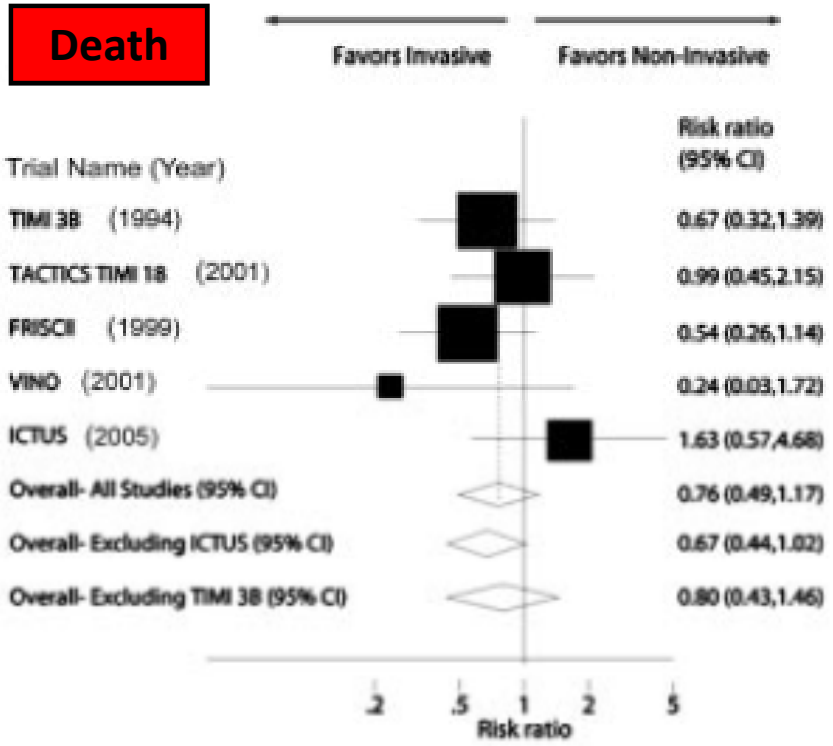
Misperception of patient risk was the most commonly cited reason for not referring patients with renal dysfunction to coronary angiography.

Should we manage patients presenting with non–ST segment elevation myocardial infarction (NSTEMI) with an early invasive strategy?

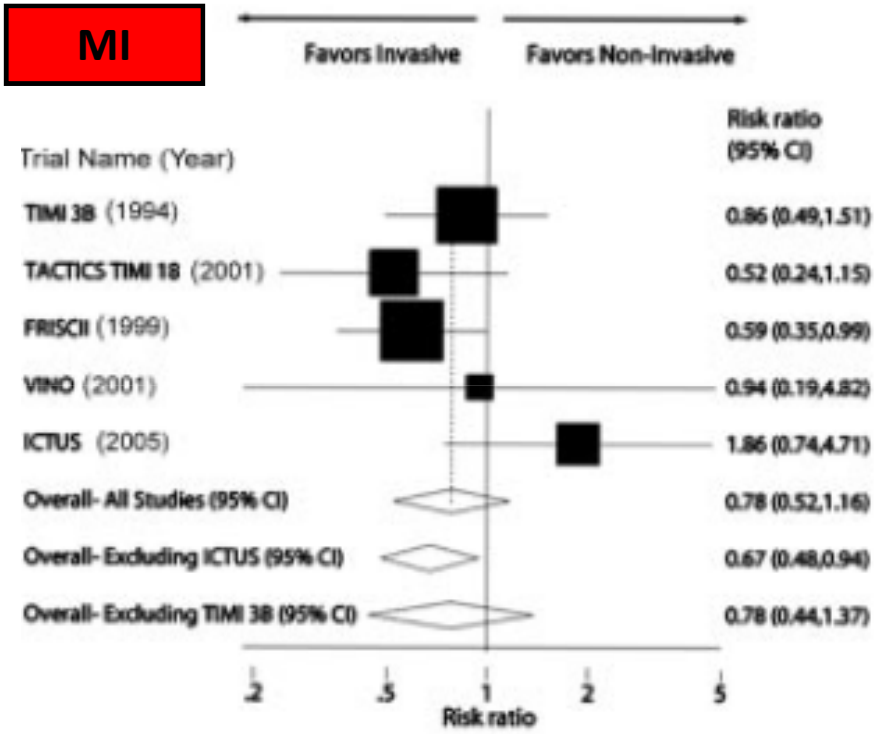
CJASN Clinical Journal of the American Society of Nephrology

Early Angiography in Patients with Chronic Kidney Disease: A Collaborative Systematic Review

Death



MI

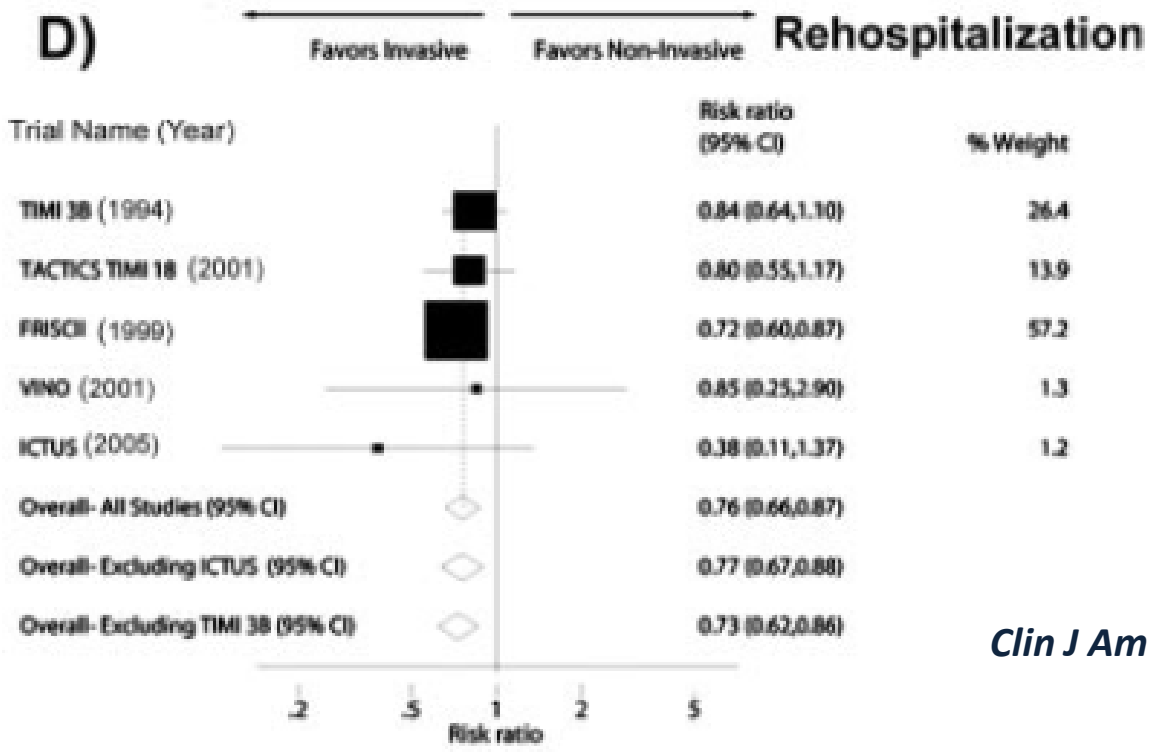


An early invasive strategy was associated with nonsignificant reductions in all-cause mortality, nonfatal MI, and a composite of death or nonfatal MI.

Clin J Am Soc Nephrol 4: 1032–1043, 2009.

CJASN Clinical Journal of the American Society of Nephrology

Early Angiography in Patients with Chronic Kidney Disease: A Collaborative Systematic Review



An invasive strategy could prevent up to 20 deaths for every 1000 patients compared with only six deaths prevented in patients without CKD.

Clin J Am Soc Nephrol 4: 1032–1043, 2009.

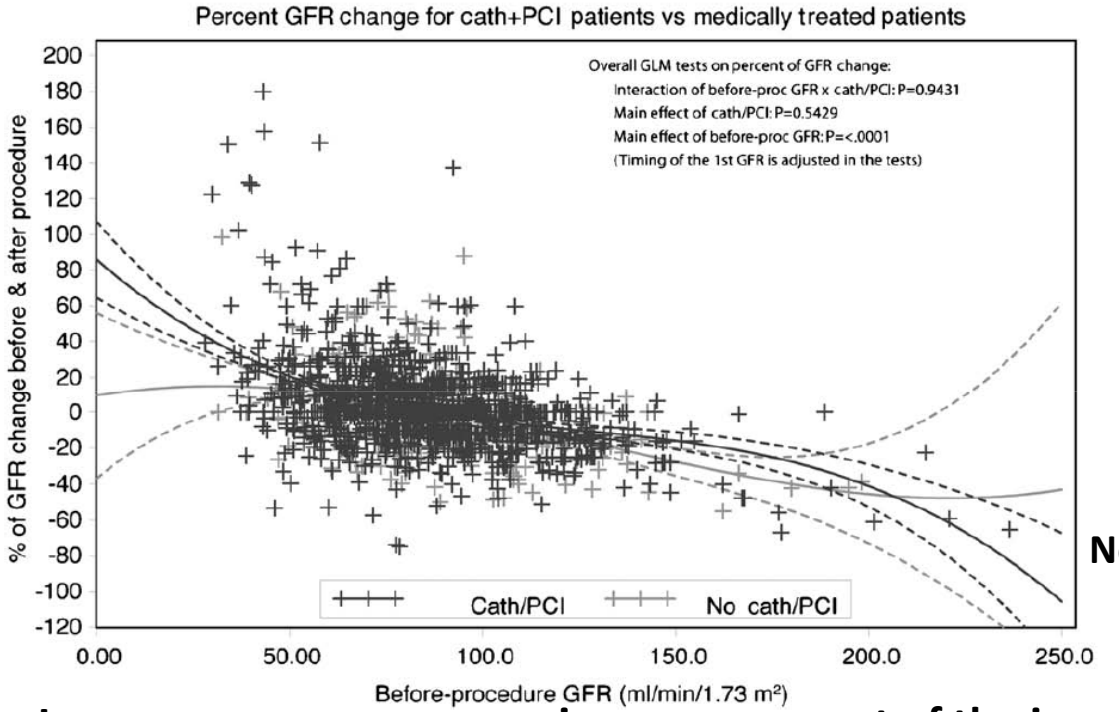
The invasive strategy significantly reduced rehospitalization.

ndt NEPHROLOGY DIALYSIS TRANSPLANTATION

Mortality, kidney disease and cardiac procedures following acute coronary syndrome

Jula K. Inrig[1], Uptal D. Patel[1], Libbie P. Briley[2], Lilin She[1], Barbara S. Gillespie[2]
J. Donald Easton[3], Eric J. Topol[4] and Lynda A. Szczech[1]

Among subjects with CKD in this study, the risk of death greatly outweighed the risk of further reduction in eGFR or development of ESRD



Among subjects with CKD, there was no increased risk of a long-term decrease in renal function following cath ± PCI.

Nephrol Dial Transplant (2008) 23: 934–940

In summary, more aggressive management of the increased cardiovascular risk in CKD patients is clearly needed and *the presence of CKD should not preclude the use of potentially beneficial diagnostic and therapeutic interventions.*

2012 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction (Updating the 2007 Guideline and Replacing the 2011 Focused Update): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY FOUNDATION

2012 Focused Update Recommendations	2012 Comments
Class I	
1. Creatinine clearance should be estimated in UA/NSTEMI patients and the doses of renally cleared medications *should be adjusted according to the pharmacokinetic data* for specific medications.162,16 *(Level of Evidence: B)*	2011 recommendation remains current.
2. Patients undergoing cardiac catheterization with receipt of contrast media *should receive adequate preparatory hydration*.164,165 *(Level of Evidence: B)*	2011 recommendation remains current.
3. Calculation of the contrast volume to creatinine clearance ratio is useful *to predict the maximum volume of contrast media that can be given* without significantly increasing the risk of contrast-associated nephropathy.166,167 *(Level of Evidence: B)*	2011 recommendation remains current.

2012 Focused Update Recommendations	2012 Comments
Class IIa 1. An invasive strategy is reasonable in patients with mild (stage 2) and moderate (stage 3) CKD.162,163,168,169 *(Level of Evidence: B)* *(There are insufficient data on benefit/risk of invasive strategy in UA/NSTEMI patients with advanced CKD stages 4, 5.)*	2011 recommendation remains current.

- Our recommendation is that an early invasive strategy (ie, diagnostic angiography with intent to perform revascularization) *is a reasonable strategy in patients with mild and moderate CKD*
- Clinicians should exercise judgment in all populations with impaired kidney function when considering whether to implement an invasive strategy. Such implementation should be considered only after careful assessment of the risks, benefits, and alternatives for each individual patient.

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

European Heart Journal (2011) 32, 2999–3054

Recommendations	Class Level
Kidney function should be assessed by CrCl or eGFR in patients with NSTE-ACS, with special attention to elderly people, women, and patients with low body weight, as near normal serum creatinine levels may be associated with lower than expected CrCl and eGFR levels.	I C
In patients with NSTE-ACS and CKD considered for invasive strategy, ***hydration and low- or iso-osmolar contrast medium at low volume (<4 mL/kg) are recommended***	I B
CABG or PCI is recommended in patients with CKD amenable to revascularization ***after careful assessment of the risk–benefit ratio in relation to the severity of renal dysfunction.***	I B

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

European Heart Journal (2011) 32, 2999–3054

Recommendations	Class Level
Patients with NSTE-ACS and CKD should receive the same first-line antithrombotic treatment as patients devoid of CKD, with appropriate dose adjustments according to the severity of renal dysfunction.	I B
Depending on the degree of renal dysfunction, dose adjustment or switch to UFH with fondaparinux, enoxaparin, bivalirudin, as well as dose adjustment with small molecule GP IIb/IIIa receptor inhibitors are indicated.	I B
UFH infusion adjusted to aPTT is recommended when CrCl is <30 mL/min or eGFR is <30 mL/min/1.73 m2 with most anticoagulants (fondaparinux <20 mL/min).	I C

Reperfusion in Patients with Renal Dysfunction after presentation With ST-Segment Elevation

✓***Renal impairment altered both the frequency and type of therapy given in patients presenting with a STEMI within 12 h of symptom onset.***

✓**Despite the proven effectiveness of reperfusion therapy in the general population, *significantly less is known about reperfusion therapy in patients with CKD or ESRD*, because these patients have generally been excluded from randomized trials.**

Original Article | Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2009.02204.x

Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: data from the SWEDEHEART register

K. Szummer[1], P. Lundman[2], S. H. Jacobson[3], S. Schön[4], J. Lindbäck[5], U. Stenestrand[6], L. Wallentin[5] & T. Jernberg[1], for SWEDEHEART

Reperfusion in STEMI		N	Reperfusion (%)	Crude OR	95% CI	Adjusted OR	95% CI
eGFR	≥90	4174	77.3	1.00	–	1.00	–
	60–89	7082	76.0	0.93	0.86–1.02	1.06	0.97–1.17
	30–59	2365	68.2	0.61	0.54–0.68	1.08	0.95–1.23
	15–29	204	53.4	0.34	0.26–0.46	0.71	0.51–0.97
	<15/dialysis	81	49.4	0.26	0.18–0.38	0.49	0.31–0.79

The likelihood of receiving reperfusion therapy for STEMI was similar in patients with normal-to-moderate renal dysfunction, but decreased in severe renal dysfunction or renal failure.

- **With decreasing renal function the use of reperfusion therapy declined from 77.3% (normal) to 49.4% (renal failure)**

J InternMed2010;268:40–49.

Original Article | Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2009.02204.x

Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: data from the SWEDEHEART register

K. Szummer[1], P. Lundman[2], S. H. Jacobson[3], S. Schön[4], J. Lindbäck[5], U. Stenestrand[6], L. Wallentin[5] & T. Jernberg[1], for SWEDEHEART

With lower renal function more patients received fibrinolysis and fewer had primary PCI.

Primary PCI versus thrombolysis in STEMI		N	Primary PCI (%)	Crude OR	95% CI	Adjusted OR	95% CI
eGFR	≥90	3225	70.8	1.00	–	1.00	–
	60–89	5382	61.3	0.65	0.60–0.71	0.70	0.63–0.77
	30–59	1612	56.5	0.55	0.49–0.62	0.65	0.56–0.74
	15–29	109	59.6	0.67	0.46–0.96	0.87	0.58–1.32
	<15/dialysis	40	42.5	0.34	0.20–0.59	0.41	0.21–0.79

Reperfusion therapy shifted from primary percutaneous coronary intervention in 71% of patients with normal renal function to fibrinolysis in 58% of those with renal failure.

J Am Coll Cardiol. 2013;61

Reperfusion in Patients With Renal Dysfunction After Presentation With ST-Segment Elevation or Left Bundle Branch Block

GRACE (Global Registry of Acute Coronary Events)

	Primary PCI (n = 3,395)	Fibrinolysis (n = 3,790)	Neither (n = 5,332)
Hospital mortality			
Normal renal function 268/9,076 (3.0%)	1.9% 51/2,699	3.1% 91/2,928	3.7% 126/3,449
Moderate renal dysfunction 426/2,974 (14.3%)	13.6% 85/624	13.3% 105/788	15.1% 236/1,562
Severe renal dysfunction 146/467 (31.3%)	29.2% 21/72	32.4% 24/74	31.5% 101/321
All patients	157/3,395	220/3,790	463/5,332
6-month mortality			
Normal renal function 160/6,635 (2.4%)	32/1,894 1.7%	36/2,236 1.6%	92/2,505 3.7%
Moderate renal dysfunction 161/1,977 (8.1%)	14/398 3.5%	26/555 4.7%	121/1,024 11.8%
Severe renal dysfunction 41/229 (17.9%)	8/36 22.2%	10/43 23.3%	23/150 15.3%
All patients 362/8,841 (4.1%)	54/2,328 2.3%	72/2,834 2.5%	236/3,679 6.4%

This study suggests that patients with moderate, but not severe, CKD might benefit from primary PCI in an acute STEMI.

Additionally, this study demonstrates less risk of complications of stroke with primary PCI in patients with moderate or severe CKD when compared with fibrinolytic therapy.

J Am Coll Cardiol Intv 2009;2:26-33.

ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC)

European Heart Journal (2012) 33, 2569–2619

✓Decisions on reperfusion in patients with STEMI have to be made before any assessment of renal function is available, but it is important to estimate the glomerular filtration rate as soon as possible after admission.

✓*Ensuring proper hydration* during and after primary PCI, and limiting the dose of contrast agents, are important in minimizing the risk of contrast-induced nephropathy.

✓ACS patients with chronic kidney *disease are frequently overdosed with antithrombotics, leading to increased bleeding risk.*

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Table 18 Initial dosing of antithrombotic agents in patients with chronic kidney disease (estimated creatinine clearance <60 mL/min)

	Recommendation
Aspirin	No dose adjustment.
Clopidogrel	No dose adjustment.
Prasugrel	No dose adjustment. No experience with end-stage renal disease/dialysis.
Ticagrelor	No dose adjustment. No experience with end-stage renal disease/dialysis.
Enoxaparin	No adjustment of bolus dose. Following thrombolysis, in patients with creatinine clearance <30 mL/min, the s.c. doses are given once every 24 h.
Unfractionated heparin	No adjustment of bolus dose.
Fondaparinux	No dose adjustment. No experience in patients with end-stage renal disease or dialysis patients.

In patients with known or anticipated reduction of renal function, several antithrombotic agents should be either withheld or their doses reduced appropriately

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Bivalirudin	• In patients with moderate renal insufficiency (GFR 30–59 mL/min) a lower initial infusion rate of 1.4 mg/kg/h should be given. The bolus dose should not be changed. • In patients with severe renal insufficiency (GFR <30 mL/min) and in dialysis-dependent patients bivalirudin is contraindicated.
Abciximab	No specific recommendation. Careful consideration of bleeding risk.
Eptifibatide	• In patients with moderate renal insufficiency (GFR ≥30 to <50 mL/min), an i.v. bolus of 180 μg should be administered followed by a continuous infusion dose of 1.0 μg/kg/min for the duration of therapy. • In patients with severe renal insufficiency (GFR <30 mL/min) eptifibatide is contraindicated.
Tirofiban	In patients with severe renal insufficiency (GFR <30 mL/min) the infusion dose should be reduced to 50%.

In patients with known or anticipated reduction of renal function, *several antithrombotic agents should be either withheld or their doses reduced appropriately*

Coronary artery disease in CKD or ESRD

To dilate or not to dilate?

PCI in CKD

Despite similar angiographic success rates, procedural and clinical success rates are lower in patients with CKD

- ❖**CKD: strong predictor of mortality / MACE in a dose-dependent fashion during and after PCI**
- ❖**higher incidence of bleeding, vascular complications**
- ❖**CKD: higher frequency of risk factors predisposing to worse outcome**
- ❖**DES HAVE NOT NEGATED THE DETRIMENTAL EFFECT OF CKD**

Risk: benefit analysis

Owing to the increased risk of these complications with PCI in patients with CKD, *a rigorous assessment of the potential benefits of PCI over medical therapy is paramount.*

Strategies

- Appropriate Indications
- Optimal interventional techniques
- MULTIDISCIPLINARY APPROACH!!!


Choice, not circumstances, determines your success
SUCCESS

Contrast-Induced Nephropathy

❖**New onset or exacerbation of renal dysfunction after contrast administration in the absence of other causes:**

- **increase by > 25% *or***
- ***absolute increase of > 0.5 mg/dL***

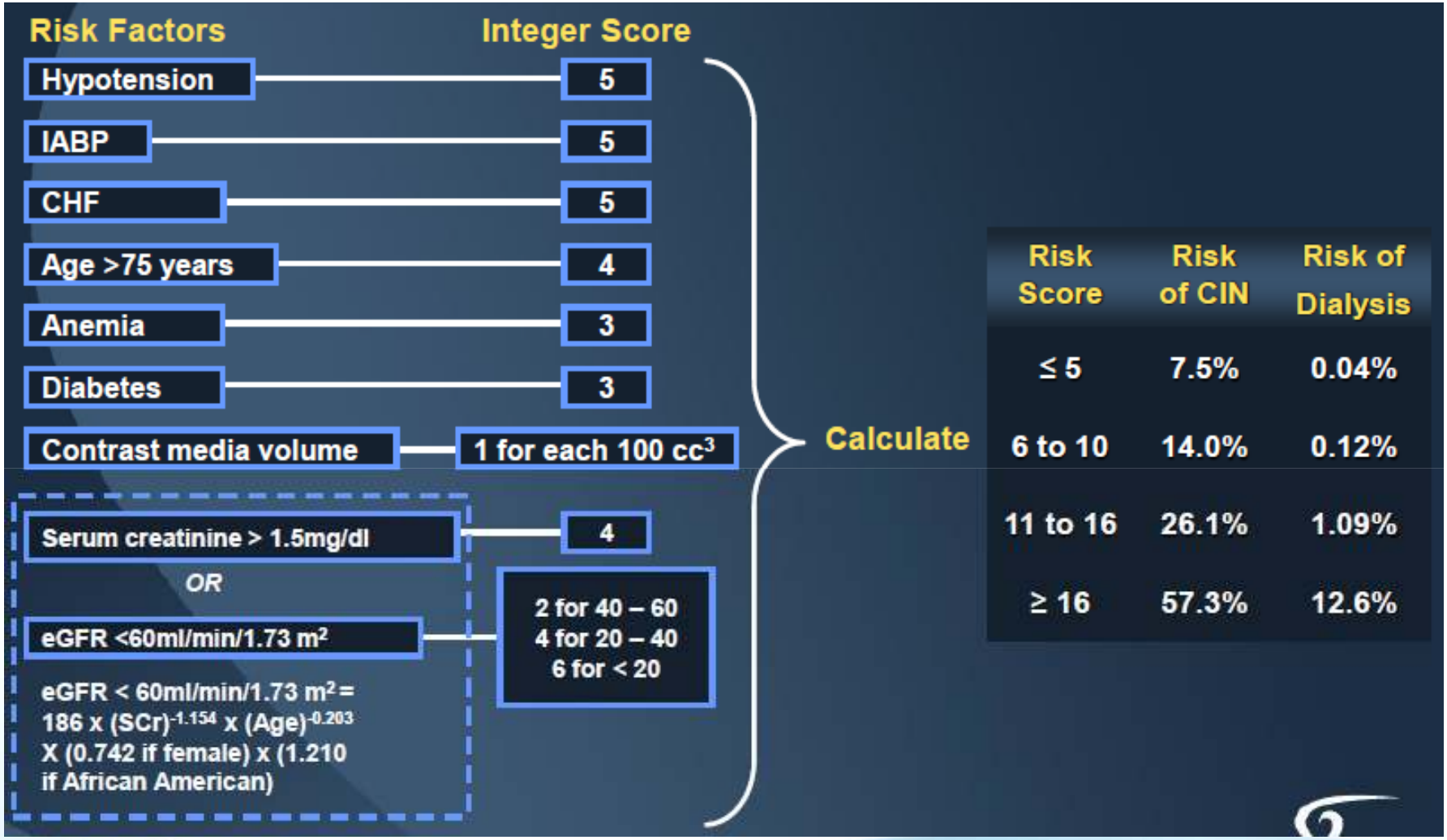
from baseline serum creatinine

❖**Occurs 24 to 48 hrs post–contrast exposure, with creatinine peaking 5 to 7 days later and normalizing within 7 to 10 days in most cases**

Risk Factors for the Development of Contrast-Induced Nephropathy

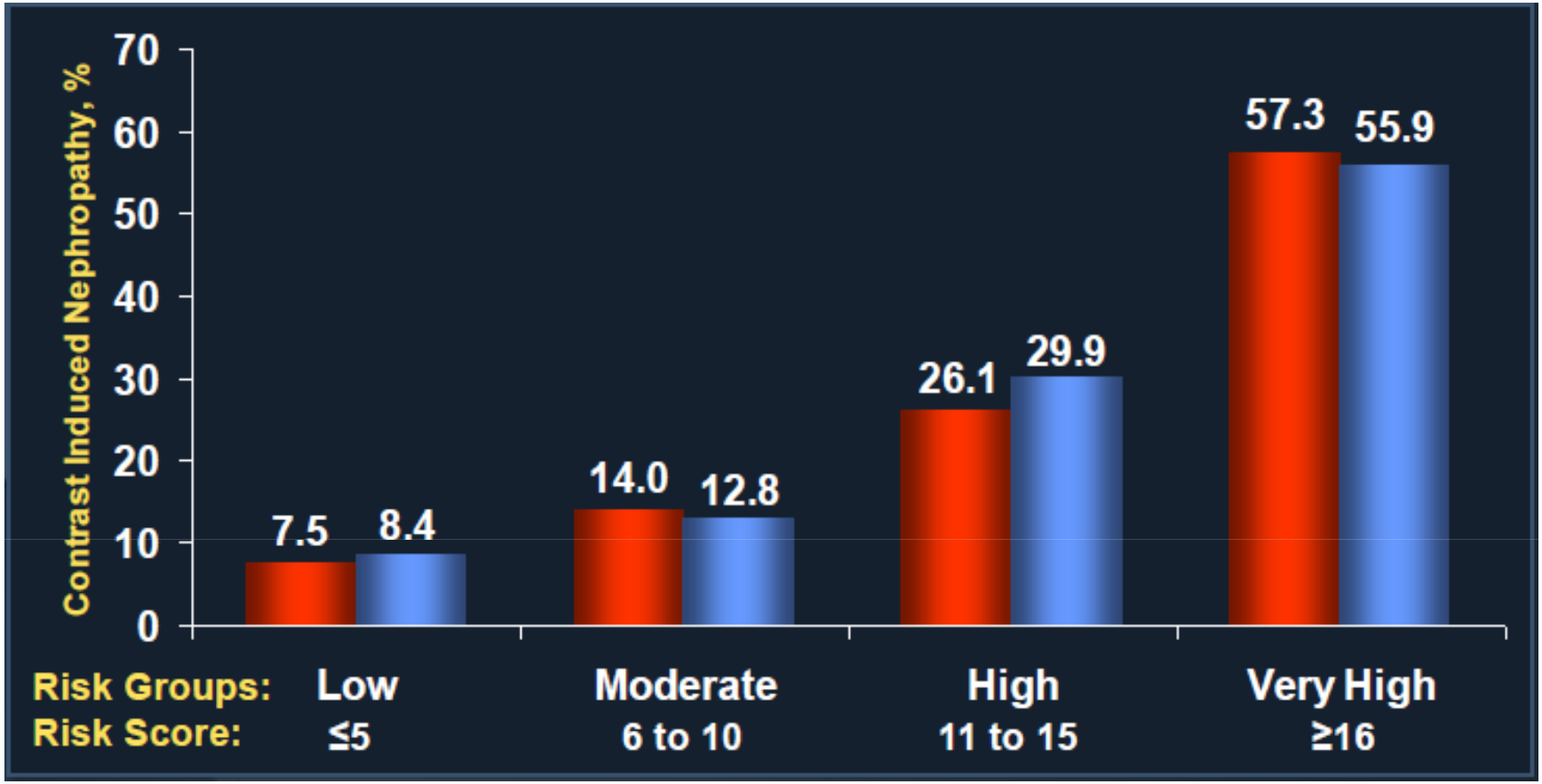
Fixed (non-modifiable) risk factors	Modifiable risk factors
Pre-existing renal failure	Volume and type of contrast medium
Diabetes mellitus	Multiple contrast injections within 72 hours
Advanced congestive heart failure	Hemodynamic instability
Reduced left ventricular ejection fraction	Dehydration
Acute myocardial infarction	Anemia
Cardiogenic shock	Intra-aortic balloon pump
Renal transplant	Low serum albumin level (<35 g/L)
	Angiotensin converting enzyme inhibitors
	Diuretics
	Nephrotoxic drugs (nonsteroidal anti-inflammatory agents, antibiotics, cyclosporine, etc.)

Scheme to Define CIN Risk Score



Mehran et al. *JACC 2004;44:1393-1399.*

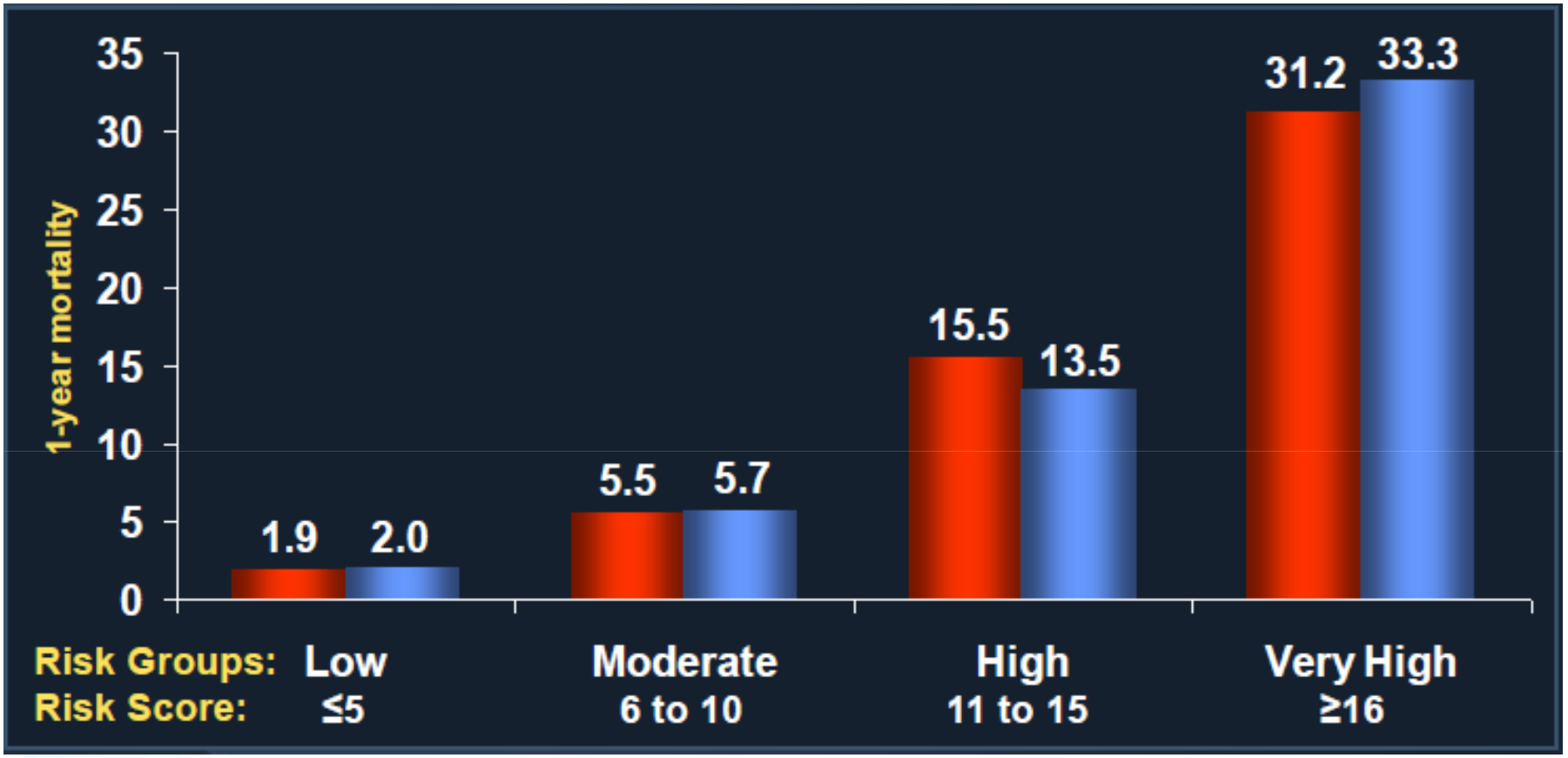
CIN Risk Score



CIN risk score derived from the development dataset predicted this complication in the validation set. (Red bars = development dataset; blue bars = validation dataset.)

Mehran et al. JACC 2004;44: 1393-1399.

CIN Risk Score & 1-year Mortality



Mehran et al. *JACC 2004;44: 1393-1399.*

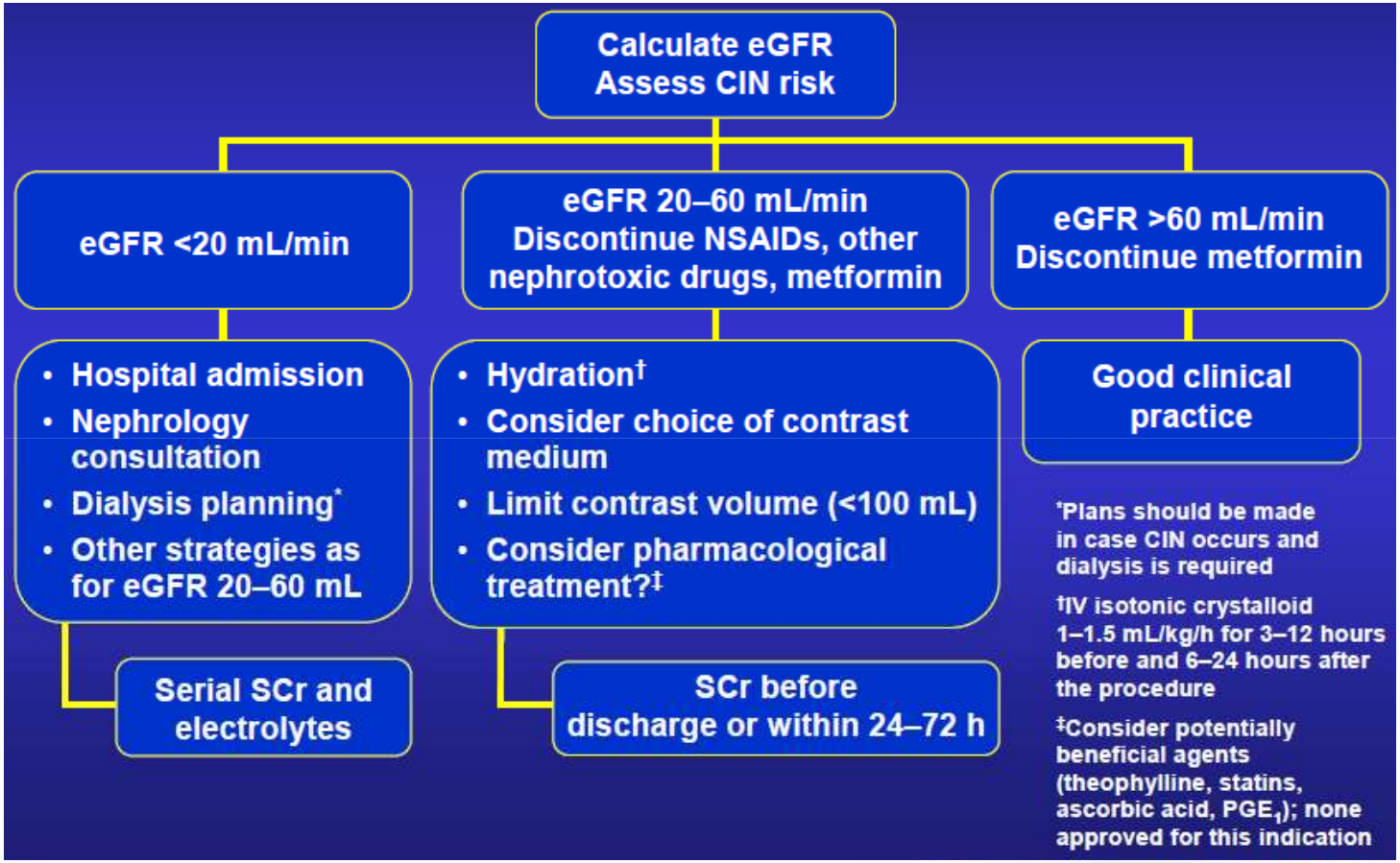
Preventive measures pre procedure, as well as careful post procedure management should be routine in all patients

- Hydration pre-PCI (12 hours recommended in high risk pts)
- D/C nephrotoxic drugs (NSAIDS, antibiotics, etc)
- Limit contrast agent volume
- No Role for n-acetylcysteine
- No Role for IV Fenoldopam
- Sodium bicarbonate probably not useful
- Low-osmolar agents are better than high-osmolar
- No powerful evidence that iso-osmolar is superior to low-osmolar in protecting against CIN

Recommendations for prevention of contrast-induced nephropathy

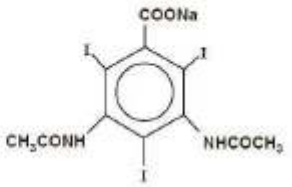
Intervention	Dose	Class[a]	Level[b]
All patients with CKD			
OMT (including statins, β-blockers, and ACE inhibitors or sartans) is recommended.	According to clinical indications.	I	A
Hydration with isotonic saline is recommended.	mL/kg/h 2 h before and continued for 24 h after the procedure (0.5 mL/kg/h if EF <35% or NYHA >2).	I	A
N-Acetylcysteine administration may be considered.	600–1200 mg 24 h before and continued for 24 h after the procedure	IIb	A
Infusion of sodium bicarbonate 0.04% may be considered.	h before: bolus = body weight in kg × 0.462 mEq i.v. infusion for 6 h after the procedure = body weight in kg × 0.154 mEq per hour.	IIb	A
Patients with mild, moderate, or severe CKD			
Use of LOCM or IOCM is recommended.	<350 mL or <4 mL/kg	I[d]	A[d]
Patients with severe CKD			
Prophylactic haemofiltration 6 h before complex PCI should be considered.	Fluid replacement rate 1000 mL/h without weight loss and saline hydration, continued for 24 h after the procedure.	IIa	B
Elective haemodialysis is not recommended as a preventive measure.		III	B

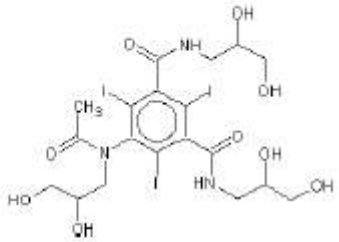
Algorithm for Management of Patients Receiving Iodinated CM

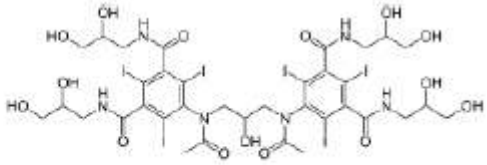


TYPE OF CM

Class of Contrast Agent	Type of Contrast Agent	Iodine/Particle Ratio	Viscosity (cPs at 37°C)	Osmolality (mOsm/kg H_2O)
High-osmolar monomers (ionic)	Diatrizoate (Renografin)	1.5	2.3	1870
	Ioxithalamate (Telebrix)	1.5	2.5	2130
Low-osmolar dimers (ionic)	Ioxaglate (Hexabrix)	3	7.5	600
Low-osmolar monomers (nonionic)	Iohexol (Omnipaque)	3	10.4	780
	Iomeprol (Iomeron)	3	12.6	620
	Ioversol (Optiray)	3	9	790
	Iopromide (Ultravist)	3	10	770
Iso-osmolar dimers	Iodixanol (Visipaque)	6	11.8	290
(nonionic)	Iotrolan (Isovist)	6	8.5	290







Management decisions in patients with renal dysfunction are complex and the reasons for the observed undertreatment are likely multifactorial. Various factors, such as overestimation of treatment-associated mortality and morbidity (e.g. contrast nephropathy and bleeding), concerns over co-morbidities, lack of definitive clinical trial data, under recognition of patient's poor prognosis, and underestimation of treatment benefit likely all play a role. Moreover, in-hospital mortality and treatment-associated complications may be higher with an early-invasive approach in these patients.28 These immediate risks may be more evident than the potential for improvement in long-term outcomes,28 and therefore have a greater impact on clinical decision-making

In summary, the use of stents and particularly drugeluting stents has decreased the rates of in-stent restenosis, but these rates remain higher than in patients with normal renal function.

Randomized Comparison of Xience V and Multi-Link Vision Coronary Stents in the Same Multivessel Patient With Chronic Kidney Disease (RENAL-DES) Study

Tomai F. Circulation. 2014;129:1104-111

In 215 patients, 512 coronary vessels were successfully treated with the randomly assigned DES (n=257) or BMS (n=255). At 1 year, the rate of ischemia-driven target vessel revascularization for DES and BMS groups was 2.7% (95% confidence interval, 1.1%–5.6%) and 11.4% (95% confidence interval, 7.8% to 16%), respectively, *P*<0.001. For the multivariate analysis, independent predictors of the ischemia-driven target vessel revascularization were BMS implantation (odds ratio, 4.95; 95% confidence interval, 2.1–11.6; *P*<0.001) and vessel size (odds ratio, 0.32; 95% confidence interval, 0.1–0.7; *P*=0.006).

This is the first randomized trial showing a reduction of clinical restenosis with a new-generation DES in comparison with a BMS of equal design, in patients who have chronic kidney disease with multivessel coronary artery disease.