

VALVULAR DISEASE IN CKD/ESRD

Mohamed Marwan Cardiologist University Hospital Erlangen

DISCLOSURES

• Speaker Honoraria Siemens Healthineers and Edwards Lifesciences





CONSIDERATIONS

- Differences compared to normal population ?
- Influence of CKD on natural history of valvular disease
- Diagnostics
- Prevention
- Challenges in interventional/surgical treatment
- Valvular disease and oral anticoagulation in the setting of CKD/ESRD



CARDIOVASCULAR DISEASE IN CKD/ESRD PATIENTS

- Two to four times likelihood of cardiovascular disease compared to general population
- Leading cause of Mortality in this cohort

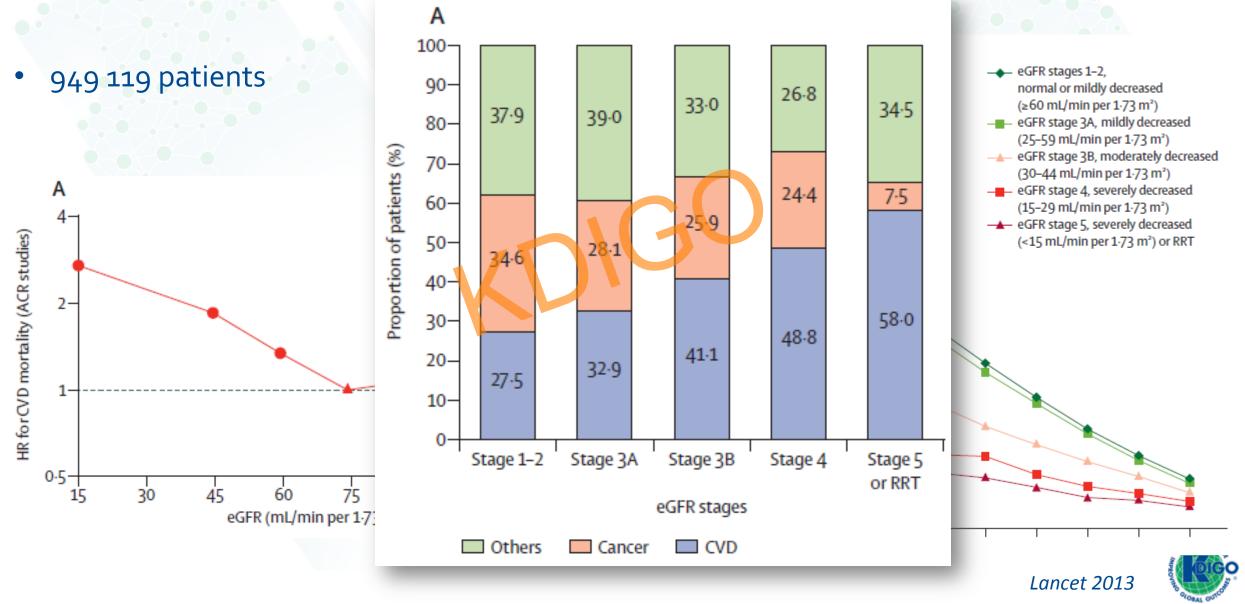
 Pathophysiology mainly related to vascular and valvular calcifications

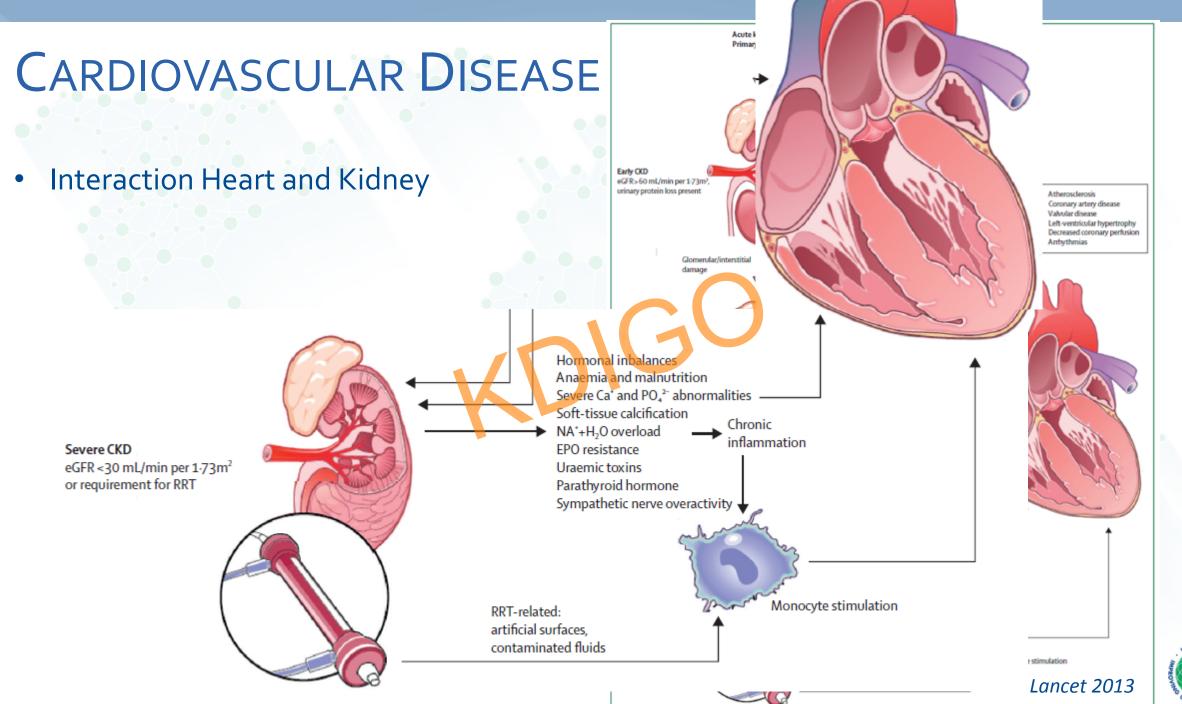


CARDIOVASCULAR DISEASE IN CKD/ESRD PATIENTS Global Cardiovascular and Renal Outcomes of Reduced GFR Global Burden of Disease 2013 GFR Collaborators, CKD Prognosis Consortium, and Global Burden of Disease Genitourinary Expert Group Due to the number of contributing authors, the authors and affiliations are listed at the end of this article. World Regi Table 2. CV and CKD mortality attributable to reduced GFR in 2013 CV Disease Global Developed AS GFR-Attributable GFR-Attributable Counts World Region Developing among All Ages Rate per 100,000 Global 1,207,453 (1,049,528 to 1,400,049) 20.8 (18.1 to 24.1) Developed 465,696 (389,760 to 544,138) 19.2 (16.2 to 22.2) Developing 741,757 (629,223 to 884,731) 21.5 (18.0 to 25.5) JASN 2017



CARDIOVASCULAR DISEASE IN CKD/ESRD PATIENTS









Primarily triggered by valvular calcification

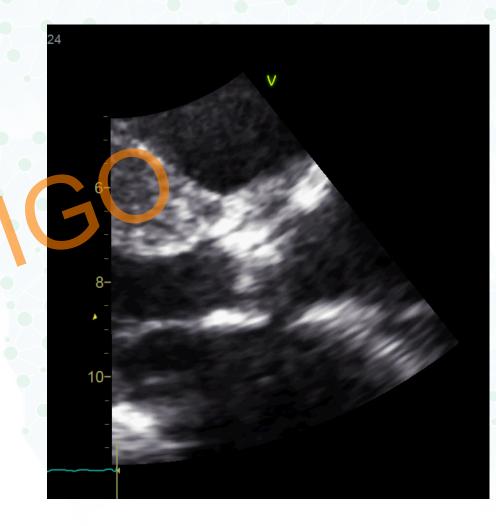
• Left sided valve affection due to higher mechanical stress

Aortic position causing predominantly stenosis

• Mitral position causing leaflet restriction/calcification presenting more frequently with mitral regurgitation and mitral stenosis

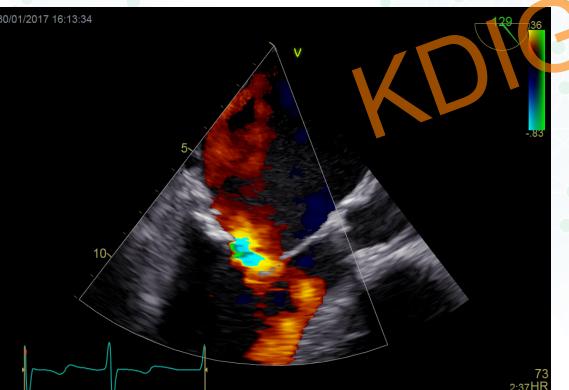


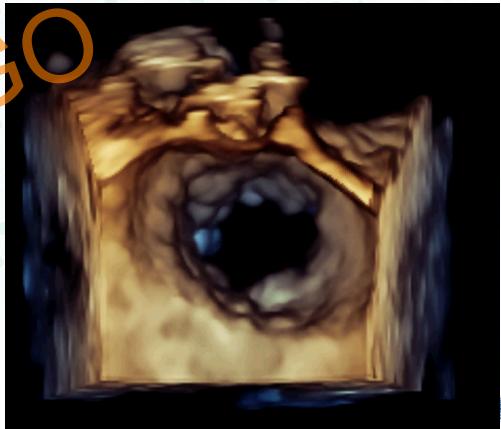
AS -> Calcification





MR —> Calcification of the annulus, mitral valve apparatus, chordae causing primary MR





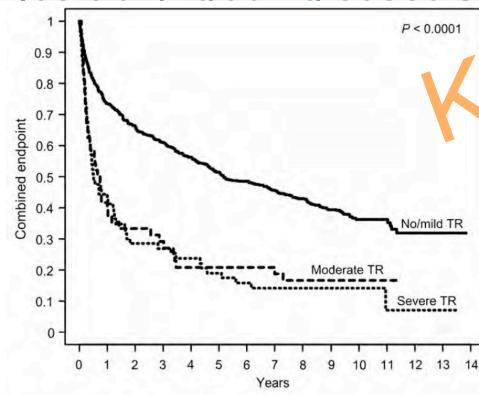


 MR —> Calcification of the annulus, mitral valve apparatus, chordae causing primary MR

Poor LV functions due to concomitant CAD , secondary MR



Right sided heart more context of pulmonary h





European Heart Journal (2013) **34**, 844–852 doi:10.1093/eurheartj/ehs465 CLINICAL RESEARCH Heart failure/cardiomyopathy

Impact of tricuspid regurgitation on survival in patients with chronic heart failure: unexpected dings of a long-term observational study

phanie Neuhold^{1,2}, Martin Huelsmann¹*, Elisabeth Pernicka³, Alexandra Graf³, na Bonderman¹, Christopher Adlbrecht¹, Thomas Binder¹, Gerald Maurer¹, ard Pacher¹, and Julia Mascherbauer¹

Conclusion

The impact of TR on the outcome in CHF patients depends on the severity of heart failure. While TR provides no additive value in advanced disease, it is associated with excess mortality in mild to moderate CHF. Whether these patients may benefit from surgical correction of TR has to be addressed in further prospective, randomized studies.

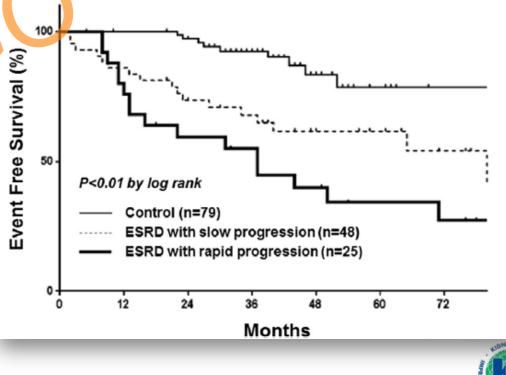




- Increased calcium deposition
- The natural history of disease is different then AS in non-CKD population: accelerated progression, younger presentation

Effect of End-Stage Renal Disease on Rate of Progression of Aortic Stenosis

Darae Kim, MD, Chi Young Shim, MD, PhD*, Geu-Ru Hong, MD, PhD, In Jeong Cho, MD, Hyuk-Jae Chang, MD, PhD, Jong-Won Ha, MD, PhD, and Namsik Chung, MD, PhD



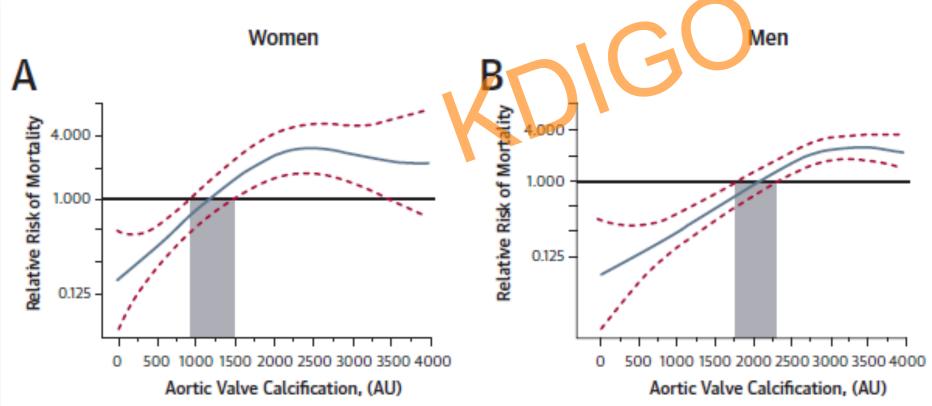


Calcium is related to outcome

Impact of Aortic Valve Calcification, as Measured by MDCT, on Survival in Patients With Aortic Stenosis

Results of an International Registry Study

Marie-Annick Clavel, DVM, PHD,* Philippe Pibarot, DVM, PHD,† David Messika-Zeitoun, MD, PHD,† Romain Canoulade. PHD.† Joseph Malouf. MD.* Shivani R. Aggarwal, MBBS,* Phillip A. Araoz, MD,*



с,† Jordan D. Miller, РнD,* Alec Vahanian, MD,‡§

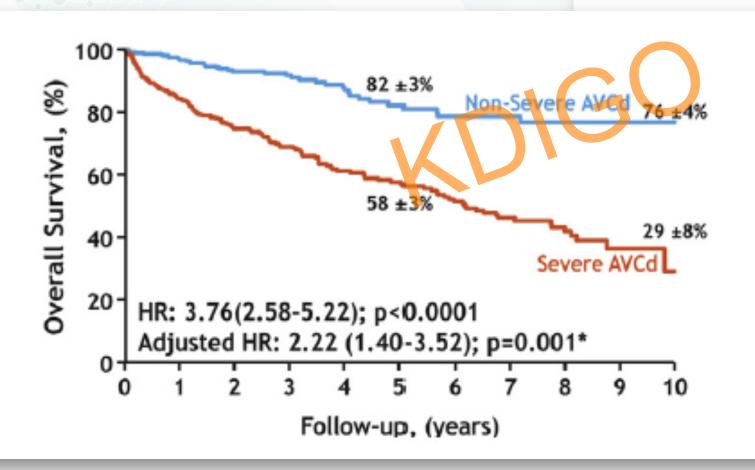
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JACC 2014

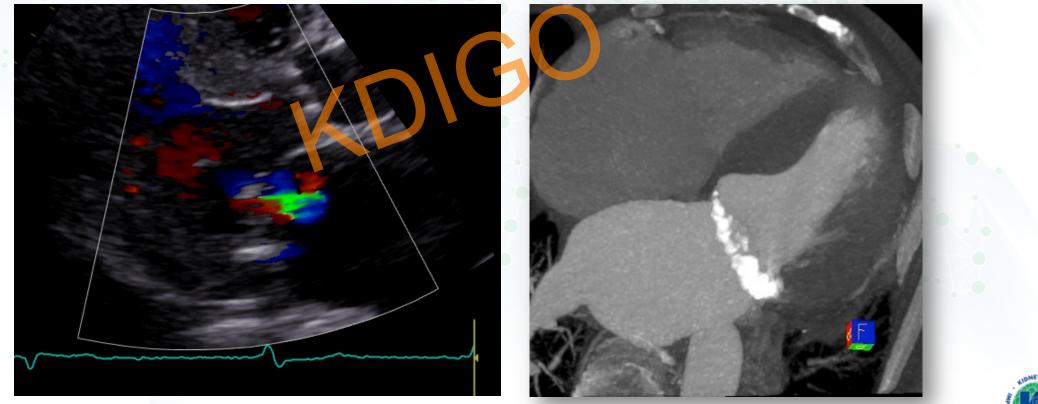
fication, (AU)

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 Mitral annular calcification with varying severity causing regurgitation or stenosis





• Embolic manifestations especially in severe forms of MAC (Caseous mitral valve calcification)

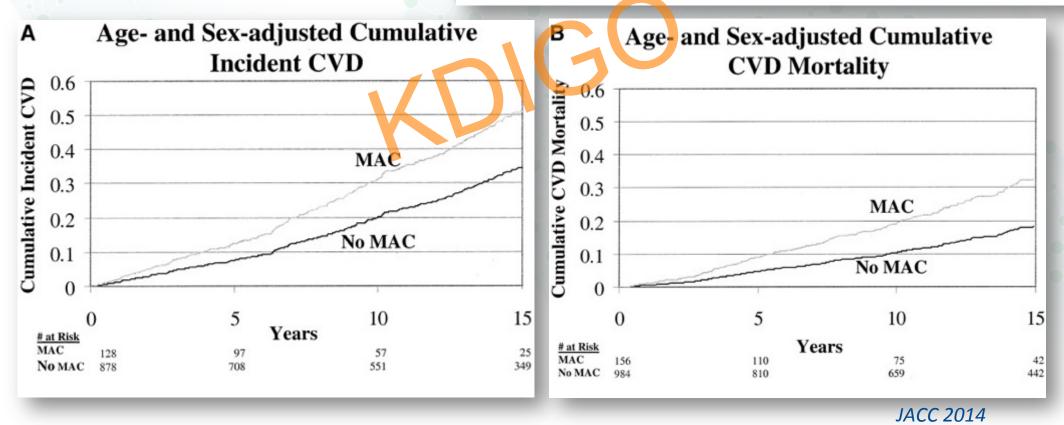




• MAC associated with CVD morbidity and mortality

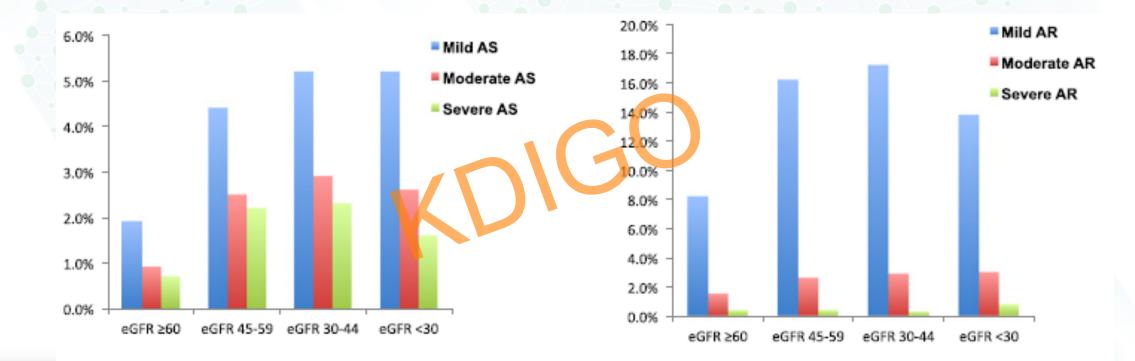
Mitral Annular Calcification Predicts Cardiovascular Morbidity and Mortality The Framingham Heart Study

Caroline S. Fox, MD, MPH; Ramachandran S. Vasan, MD; Helen Parise, ScD; Daniel Levy, MD; Christopher J. O'Donnell, MD, MPH; Ralph B. D'Agostino, PhD; Emelia J. Benjamin, MD, ScM



PREVALENCE OF LEFT-SIDED VALVULAR LESIONS IN CKD

Longitudinal data from 1999 to 2013, 78 059 patients, 30% CKD



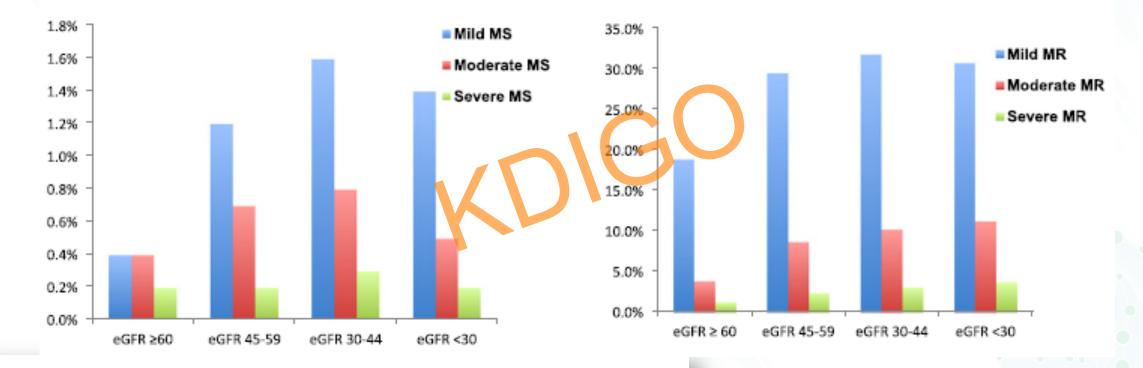
Prevalence and Outcomes of Left-Sided Valvular Heart Disease Associated With Chronic Kidney Disease

Zainab Samad, MD, MHS; Joseph A. Sivak, MD; Matthew Phelan, MS; Phillip J. Schulte, PhD; Uptal Patel, MD; Eric J. Velazquez, MD



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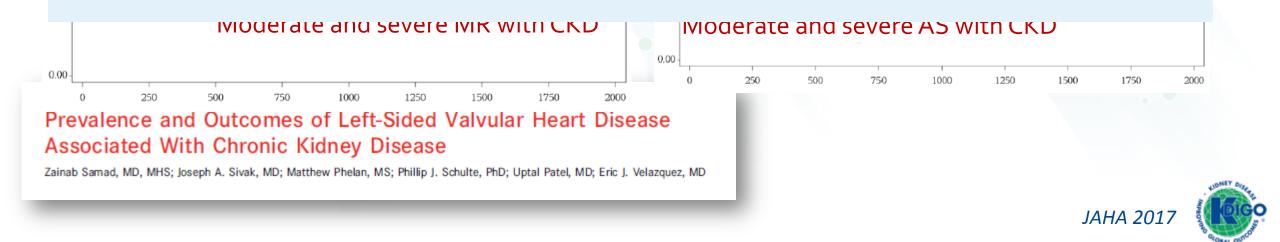


PREVALENCE OF LEFT-SIDED VALVULAR LESIONS IN CKD

Longitudinal data from 1999 to 2013, 78 059 patients, 30% CKD

- B
 Kaplan Meier curves for all levels of Mitral Regurgitation
 B
 Kaplan Meier curves for all levels of Aortic Stenosis

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 - The prevalence of at least mild left-sided valvular disease in the CKD group was more than double that in the non-CKD
 - The 5-year mortality rate of patients with at least mild AS/MR was > 50% greater in the CKD group than in the non-CKD group



DIAGNOSTIC IMAGING IN CKD/ESRD PATIENTS

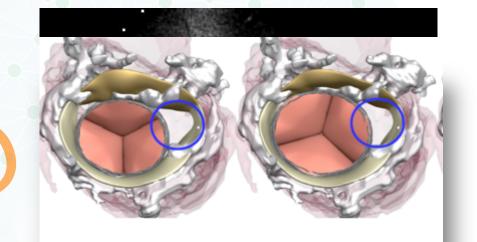


DIAGNOSTIC IMAGING IN CKD/ESRD PATIENTS

Clearly a domain of echocardiography

CT: transcatheter intervention

• MRI: only aortic regurgitation





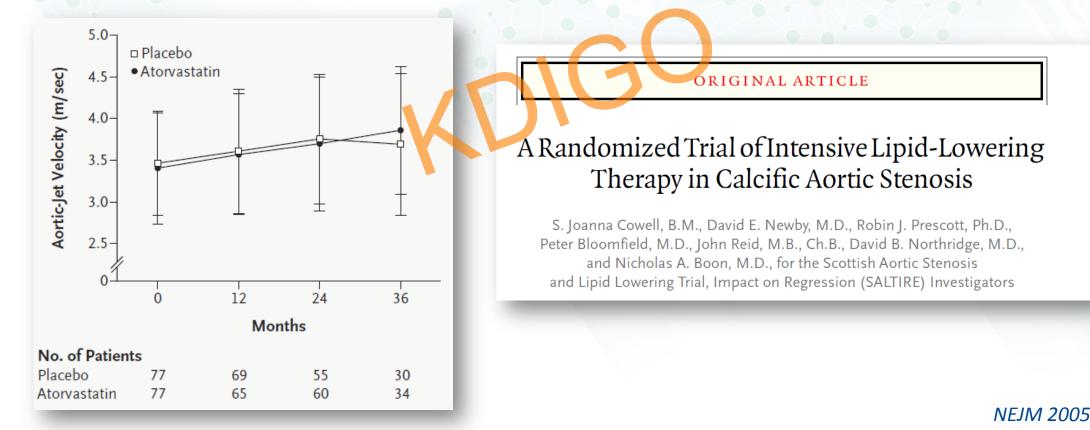
PREVENTIVE STRATEGIES IN CKD/ESRD PATIENTS

- Clustering of cardiovascular risk factors in this patient cohort
- Common disease pathways for kidney and cardiovascular
- disease
- Whether strict control of risk factors has the same benefit/ effect in CKD and non-CKD is not entirely clear
- Screening for valvular lesions in symptomatic patients



PREVENTIVE STRATEGIES IN CKD/ESRD PATIENTS

 STATINS for AS: have not proved beneficial so far in general population and Data can probably be extrapolated to CKD





TREATMENT OF VALVULAR DISEASE



TREATMENT OF VALVULAR DISEASE

 Data gap : Insufficient data for guidelines concerning management and follow-up in these patients

More treatment options with the advent of percutaneous catheter interventions

 Better definition of which CKD/ESRD patients would benefit most and which time point from intervention



TREATMENT OF AORTIC STENOSIS

Survival Surgery for Aortic stenosis 100ulative survival (%) 80 3266 patients with moderate CKD • 60 Cum 20 Normal kidney function Moderately reduced kidney function 0 15 10 5Time (years) Number at risk eGFB > 605502 2044316 9836875 nGEB 30_60_3266 1810 84.

Late Survival After Aortic Valve Replacement Moderately Reduced Kidney Function

Natalie Glaser, MD; Veronica Jackson, MD, PhD; Martin J. Holzmann, MD, PhD; Anders Franco-Cereceda, MD, PhD; Ulrik Sartipy, MD, PhD

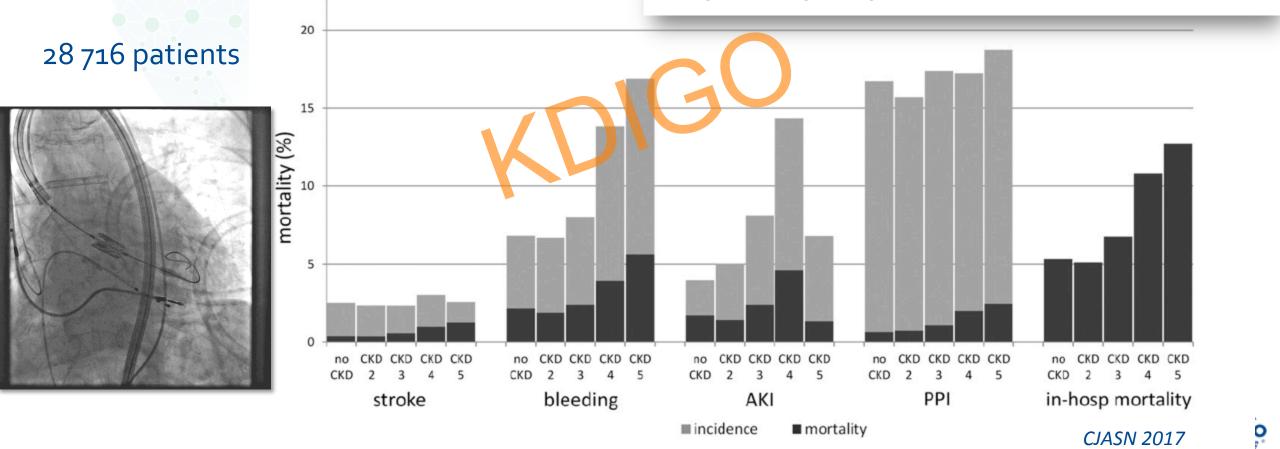


TREATMENT OF AORTIC STENOSIS

• TAVI/TAVR for Aortic stenosis in Germany

Association of CKD with Outcomes Among Patients Undergoing Transcatheter Aortic Valve Implantation

Florian Lüders,* Klaus Kaier,^{††} Gerrit Kaleschke,[§] Katrin Gebauer,* Matthias Meyborg,* Nasser M. Malyar,* Eva Freisinger,* Helmut Baumgartner,[§] Holger Reinecke,* and Jochen Reinöhl[†]



Variable	Transcatheter or surgical aortic valve replacement in pa with advanced kidney disease: A propensity score-mate analysis		
	Rajkumar D	oshi ¹	ın Jauhar ¹ Perwaiz Me
	SAVR, n = 248	35 TAVR, n = 2485	P Value
In-hospital mortality	12.9	6.2	<0.01
AKI	50.3	33	<0.01
			-0.01
Dialysis requirement	26.8	20.1	< 0.01
Dialysis requirement Blood transfusion	26.8 49.7	20.1 38.2	<0.01

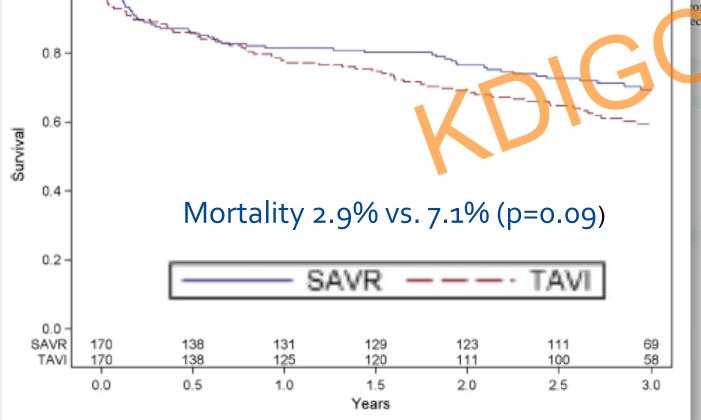


TAVI/TAVR VERSUS SURGICAL REPLACEMENT

Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement for Severe Aortic Stenosis in Patients With Chronic Kidney Disease Stages 3b to 5

> o, MS, Claudio Moretti, MD, Fabrizio D'Ascenzo, MD, Stefano Rosato, MS, ri, MD, Marco Barbanti, MD, Francesco Santini, MD, Marco Ranucci, MD, li, MD, Corrado Tamburino, MD, Francesco Onorati, MD, oro, MD, Claudio Grossi, MD, Danilo Fusco, MS, and eccia, MS, on behalf of the OBSERVANT Research Group

> > Propensity score matched patients (170)



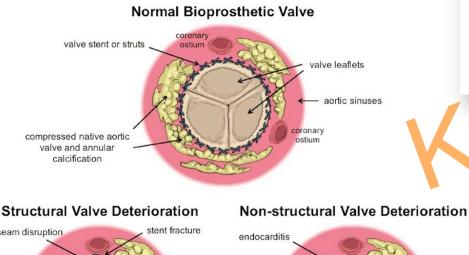
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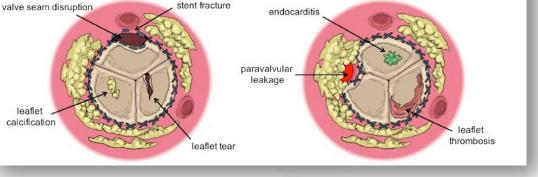
Am J Cardiol 201

CrossMark



VALVE DURABILITY





Importance of the valve durabilitylife expectancy ratio in selection of a prosthetic aortic valve

Rodrigo Bagur,^{1,2,3} Philippe Pibarot,⁴ Catherine M Otto⁵

Ideally, durability of an aortic bioprosthetic valve should outlast longevity of the patient. A patient-centred approach is of paramount importance, always considering the 'valve durability to life expectancy ratio'.

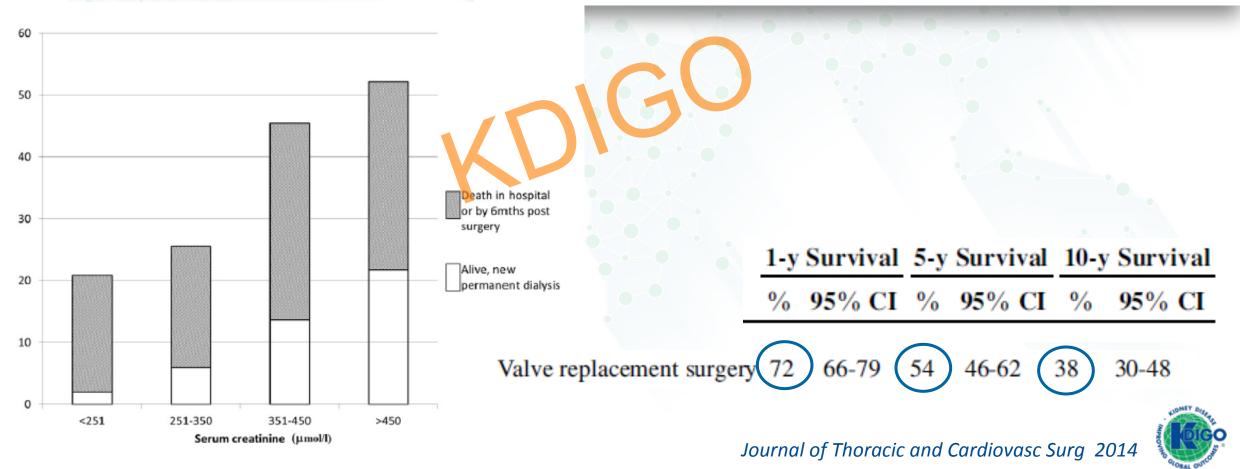


VALVE REPLACEMENT IN CKD

545 patients

Outcomes of cardiac surgery in chronic kidney disease

Mangalee Fernando, FRACP,^{a,b} Hugh S. Paterson, FRACS,^c Karen Byth, PhD,^d Benjamin M. Robinson, MBBS, MPhil,^e Hugh Wolfenden, FRACS,^f David Gracey, PhD, FRACP,^{c,g} and David Harris, MD, BS, FRACP^{c,h}

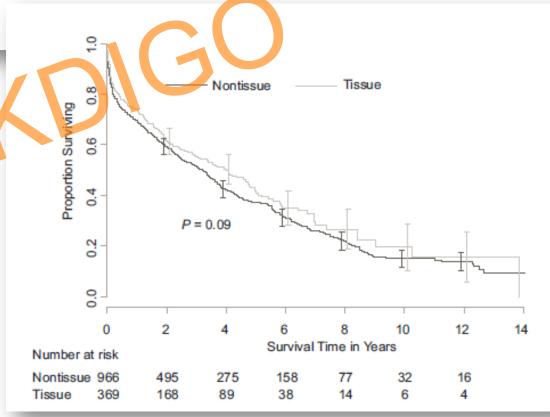


VALVE SURGERY IN RENAL TRANSPLANT PATIENTS

- 1335 transplant patients
- 75% AVR
- 20% MV
- 5% combined
- In-hospital overall mortality 14%
- 2-year mortality 40%
- Tissue valves preferred

Valvular Heart Disease

Survival of Kidney Transplantation Patients in the United States After Cardiac Valve Replacement





TAVI/TAVR IN RENAL TRANSPLANT PATIENTS

8 transplant patients

• All alive at 1 year

Transcatheter aortic valve implantation improves outcome compared to open-heart surgery in kidney transplant recipients requiring aortic valve replacement

Henrik Fox (MD)^a, Stefan Büttner (MD)^b, Katrin Hemmann (MD)^a, Aida Asbe-Vollkopf (MD)^b, Mirko Doss (MD)^c, Andres Beiras-Fernandez (MD)^c, Anton Moritz (MD)^c, Andreas M. Zeiher (MD)^a, Ernst Scheuermann (MD)^d, Helmut Geiger (MD)^b, Stephan Fichtlscherer (MD)^a, Ingeborg A. Hauser (MD)^b, Ralf Lehmann (MD)^{a,*}

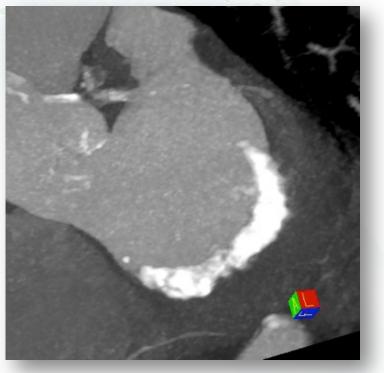
^a Department of Cardiology, Johann Wolfgang Goethe-University Frankfurt, Theodor-Stern-Kai 7, D-60590 Frankfurt, Germany ^b Department of Nephrology, Johann Wolfgang Goethe-University Frankfurt, Theodor-Stern-Kai 7, D-60590 Frankfurt, Germany ^c Department of Heart Surgery, Johann Wolfgang Goethe-University Frankfurt, Theodor-Stern-Kai 7, D-60590 Frankfurt, Germany ^d KfH Kuratorium für Dialyse und Nierentransplantation e.V. Schleusenweg 22, D-60590 Frankfurt, Germany

• Retrospective comparison to 18 patients sent for AVR, 1-year mortality 16.7%



MITRAL VALVE SURGERY

- Due to anatomical considerations with excessive calcification, mitral valve repair often not possible
- Similar to AVR, CKD/ESRD affects outcome after surgery





MITRAL VALVE SURGERY

Mitral procedure selection in patients on dialysis: Does mitral repair influence outcomes?

 Due to anatomical considerations wit often not possible

Christina M. Vassileva, MD,^a J. Matthew Brennan, MD, MPH,^b James S. Gammie, MD,^c Shubin Sheng, MS,^d Theresa Boley, MSN,^a Paramita Saha-Chaudhuri, PhD,^e and Stephen Hazelrigg, MD^a

Variable*	Overall (n = 86,563)	No dialysis $(n = 85,083)$	Dialysis (n = 1480)	P value			
Median ventilation time (h) (IQR)‡	7.5 (4.6-14.9)	7.4 (4.6-14.5)	17.1 (7.6-38.5)	<.0001			
I Denair attempted loce f	raquantly)01			
i • Repair attempted less frequently							
1)68			
^I • Repair success equally I	ikely			.53			
I Repair soccess equary i	incery)01			
I)01)01			
^I • Repair vs. Replacement did not affect short term outcome							
N)01			
Surgical mortality (%)	2.4	2.3	9.3	<.0001			
Composite morbidity and mortality (%)	16.3	15.9	40.9	<.0001			



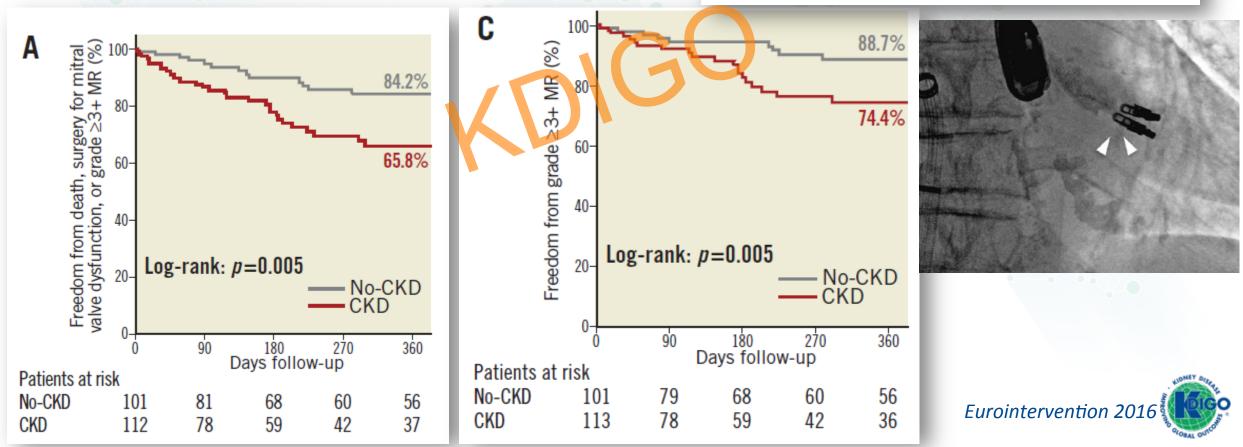
ITCVS 2014

PERCUTANEOUS TREATMENT OF MR IN CKD/ESRD

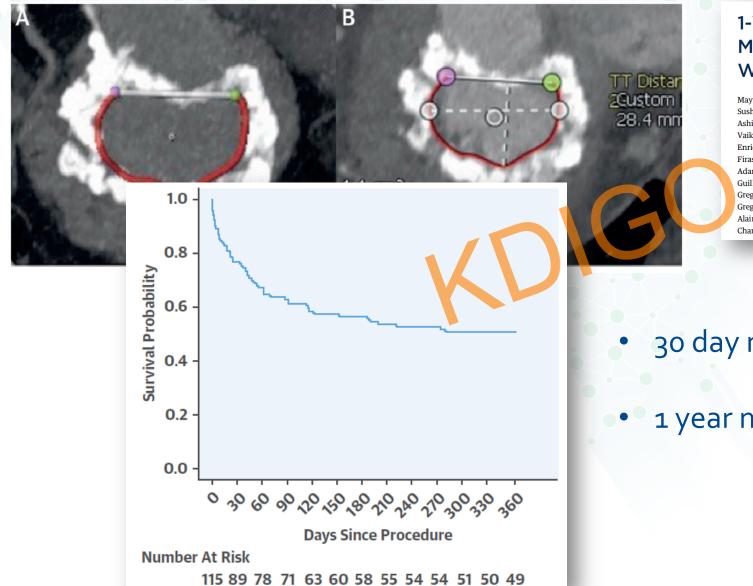
Impact of chronic kidney disease on outcomes after percutaneous mitral valve repair with the MitraClip system: insights from the GRASP registry



Yohei Ohno^{1,2}, MD; Guilherme F. Attizzani^{1,3}, MD; Davide Capodanno^{1,4}, MD, PhD; Marco Barbanti¹, MD; Stefano Cannata¹, MD; Fabio Dipasqua¹, MD; Sebastiano Immé¹, MD; Margherita Ministeri¹, MD; Anna Caggegi¹, MD; Anna M. Pistritto¹, MD; Marta Chiarandà¹, MD; Giuseppe Ronsivalle¹, MD; Sandra Giaquinta¹, MD; Sarah Mangiafico¹, MD; Salvatore Scandura¹, MD; Piera Capranzano^{1,4}, MD, PhD; Corrado Tamburino^{1,4}, MD, PhD; Carmelo Grasso^{1*}, MD



PERCUTANEOUS TREATMENT OF MR IN CKD/ESRD



1-Year Outcomes of Transcatheter Mitral Valve Replacement in Patients With Severe Mitral Annular Calcification

Mayra Guerrero, MD,^{a,*} Marina Urena, MD,^{b,*} Dominique Himbert, MD,^b Dee Dee Wang, MD,^c Mackram Eleid, MD,^d Susheel Kodali, MD,^e Isaac George, MD,^f Tarun Chakravarty, MD,^g Moses Mathur, MD,^h David Holzhey, MD, PHD,ⁱ Ashish Pershad, MD,^j H. Kenith Fang, MD,^k Daniel O'Hair, MD,¹ Noah Jones, MD,^m Vaikom S. Mahadevan, MBBS, MD,ⁿ Nicolas Dumonteil, MD,^o Josep Rodés-Cabau, MD,^p Nicolo Piazza, MD,^q Enrico Ferrari, MD,^f Daniel Ciaburri, MD,^s Mohammed Nejjari, MD,^f Augustin DeLago, MD,^u Paul Sorajja, MD,^v Firas Zahr, MD,^w Vivek Rajagopal, MD,^s Brian Whisenant, MD,^v Pinak Bipin Shah, MD,^z Jan-Malte Sinning, MD,^{aa} Adam Witkowski, MD,^{bb} Helene Eltchaninoff, MD,^{cc} Danny Dvir, MD,^{dd} Bena Martin, MD,^{ee} Guilherme F. Attizzani, MD,^{ff} Diego Gaia, MD,⁶⁸ Nagela S.V. Nunes, MD,^{hh} Amir-Ali Fasas, MD,ⁱⁱ Faraz Kerendi, MD,^{ij} Gregory Pavlides, MD,^{kk} Vijay Iyer, MD,^{il} Georges Kaddissi, MD,^{rm} Christian Witzke, MD,ⁿⁿ James Wudel, MD,^{oo} Gregory Mishkel, MD,^{pp} Bryan Raybuck, MD,^{ed} Chi Wang, PHD,^{rr} Ron Waksman, MD,⁵⁶ Igor Palacios, MD,^{tt} Alain Cribier, MD,^{cC} John Webb, MD,^{dd} Vinnie Bapat, MD,^f Mark Reisman, MD,^h Raj Makkar, MD,^g Martin Leon, MD,^e Charanjit Rihal, MD,^d Alec Vahanian, MD,^b William O'Neill, MD,^c Ted Feldman, MD^a

- 30 day mortality 25%
- 1 year mortality 53%



JACC 2018



CHOICE OF VALVE IN ESRD PATIENTS

- 5523 mechanical valves
- 1600 tissue valves

DOI 10.1111/jocs.12805

ORIGINAL ARTICLE

WILEY Cardiac Surgery

Tissue valves are preferable for patients with end-stage renal disease: an aggregate meta-analysis

Salah E. Altarabsheh, M.D.¹ | Salil V. Deo, M.S., M.Ch.^{2*} | Shannon M. Dunlay, M.S., M.D.³ | Yaqthan M. Obeidat, M.D.⁴ | Patricia J. Erwin, M.D.⁵ | Abeer Rababa'h, Ph.D.⁶ | Nagaraju Sarabhu, M.D., M.P.H.⁷ | Suparna Navale, M.S., M.P.H.⁸ | Yang Hyun Cho, M.D.⁹ | Harveen K. Lamba, M.D.¹⁰ | Alan H. Markowitz, M.D.² | Soon J. Park, M.D.²

OR, 95% Cl p-Value
1.15 [0.77; 1.72] 0.49
2.55 [1.53; 4.26] <0.01
0.32 [0.11; 0.91] 0.03

Structural valve degeneration

was present in only 0.6% patients after a tissue valve replacement. Overall survival after valve replacement was poor (median 2.61 years); valve choice did not influence this outcome (pooled HR 0.87 [0.73; 1.04]; p = 0.14).



VALVE COMPLICATIONS



PROSTHETIC VALVE ENDOCARDITIS

High Risk of Prosthetic Valve Endocarditis and Death After Valve Replacement Operations in Dialysis Patients

Danielle K. Farrington, MD, Patrick D. Kilgo, MS, Vinod H. Thourani, MD, Jesse T. Jacob, MD,* and James P. Steinberg, MD*

Department of Biostatistics and Bioinformatics, Emory University Rollins School of Public Health, Atlanta; Division of Cardiothoracic Surgery, Department of Surgery, and Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia

100-		~~~ ,		~								p<0.00
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0.25 - Nondialysis Dialysis		115 79	97 49	74 28	61 20	Num 49 13	nber left at 37 10	trisk 24 3	Dial	ysis • •	 1 1	

Outcome	Control Patients n = 139 (%)	Dialysis Patients n = 139 (%)	p Value
PVE	8 (5.8)	26 (18.7)	0.001
Definite	4 (2.9)	11 (7.9)	
Possible	4 (2.9)	15 (10.8)	
In-hospital mortality	6 (4.3)	25 (18.0)	< 0.001
30-day mortality	6 (4.3)	23 (16.6)	0.004
Overall mortality	32 (23.0)	89 (64.0)	<0.001

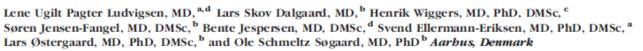
Ann Thoracic Surgery 2016

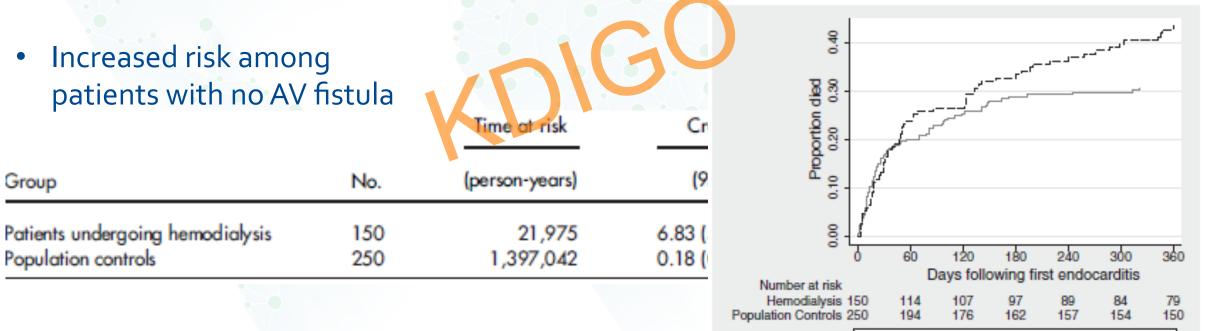


PROSTHETIC VALVE ENDOCARDITIS

- 38 fold increased risk of IE compared toage and gender matched population
- Increased risk among patients with no AV fistula

Infective endocarditis in patients receiving chronic hemodialysis: A 21-year observational cohort study in Denmark







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PROSTHETIC VALVE ENDOCARDITIS

Long-term Survival of Dialysis Patients With Bacterial Endocarditis Undergoing Valvular Replacement Surgery in the United States

Iaxwell D. Leither, MD; Gautam R. Shroff, MBBS; Shu Ding, MS; David T. Gilbertson, PhD; Charles A. Herzog, MD

0.8 Proportion Surviving 0.6 - Non-Tissue — Tissue 0 4 0.2 P = 0.420.0 2 3 5 0 Δ Years No. at Risk 269 177 85 13 Tissue 561 35 Non-tissue 706 350 238 140 30 79

10

- Predominantly Staphylococcus
 Endocarditis
- Mortality Predictors:
 - Age
 - DM as a cause of ESRD
 - Surgery during index hospitlization
 - Staph
 - Dysrhythmia



Circ 2013



• CKD patients are more prone for AF, OAK for mechanical valves

• More prone for bleeding



• More options for OAC (apart from mechanical Valves)





• Patients on RRT: no data for new OAC , VKA

• Generally, DOAC are not recommended below GFR 30 ml/min/

 Use of DOAC in AF patients with moderately reduced GFR has been shown in subgroups from RCTS to be safe and associated with less bleeding compared to VKA

Patients with CKD on VKA show less 'Time in Therapeutic Range'



Patients on R

Non-vitamin K antagonist oral anticoagulants in atrial fibrillation patients with chronic kidney disease: A systematic review and network meta-analysis

Generally, DC

^a Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy ^b Cardiovascular Department, Ferrarotto Hospital, University of Catania, Catania, Italy

Giuseppe Andò^a, Piera Capranzano^{b,*}

Conclusions: Indirect comparisons generated the hypothesis that Apixaban and Edoxaban High-Dose might be more likely associated with a better net clinical profile in AF patients with moderate CKD. These findings may potentially guide physicians in selecting the most appropriate NOAC for each patient, while waiting for dedicated evidences.



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Valvular disease in CKD/ESRD is common predominantly caused by excessive calcification

 Left-sided valvular disease (AS, MR) is eignificantly in her in CKD compared to non-CKD population and is associated with highly compared y

- For both surgical and interventional treatment, CKD patients show worse outcome compared to non-GKD populations
- TAVI/TAVR in the centext of AS in CKD seems to be associated with better outcome compared to surgery (Mortality, AKI, Hospital Stay)



- Valvular disease in CKD/ESRD is common predominantly caused by excessive calcification
- Left-sided valvular disease (AS, MR) is significantly higher in CKD compared to non-CKD population and is associated with worse outcome
- For both surgical and interventional treatment, CKD patients show worse outcome compared to non-GKD populations
- TAVI/TAVR in the context of AS in CKD seems to be associated with better outcome compared to surgery (Mortality, AKI, Hospital Stay)



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