Valvular Disease in CKD/ESRD

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Cardiologist
University Hospital Erlangen
• 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
Global Cardiovascular and Renal Outcomes of Reduced GFR

Due to the number of contributing authors, the authors and affiliations are listed at the end of this article.

Table 2. CV and CKD mortality attributable to reduced GFR in 2013

<table>
<thead>
<tr>
<th>World Region</th>
<th>GFR-Attributable Counts among All Ages</th>
<th>CV Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>AS GFR-Attributable Rate per 100,000</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Global</td>
<td>1,207,453 (1,049,528 to 1,400,049)</td>
<td>20.8 (18.1 to 24.1)</td>
</tr>
<tr>
<td>Developed</td>
<td>465,696 (389,760 to 544,138)</td>
<td>19.2 (16.2 to 22.2)</td>
</tr>
<tr>
<td>Developing</td>
<td>741,757 (629,223 to 884,731)</td>
<td>21.5 (18.0 to 25.5)</td>
</tr>
</tbody>
</table>
CARDIOVASCULAR DISEASE IN CKD/ESRD PATIENTS

- 949,119 patients

Lancet 2013
CARDIOVASCULAR DISEASE

• Interaction Heart and Kidney
Valvular affection in CKD/ESRD Patients
Valvular affection 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
VALVULAR AFFECTION IN CKD/ESRD PATIENTS

• AS → Calcification
VALVULAR AFFECTION IN CKD/ESRD PATIENTS

- MR → Calcification of the annulus, mitral valve apparatus, chordae causing primary MR
Valvular affection in CKD/ESRD Patients

- MR → Calcification of the annulus, mitral valve apparatus, chordae causing primary MR

Poor LV functions due to concomitant CAD, secondary MR
**Valvular affection in CKD/ESRD Patients**

- Right sided heart more commonly affected in context of pulmonary hypertension due to left sided lesion, high volume status.

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

*Stephanie Neuhold*¹, *Martin Huelsmann*¹, *Elisabeth Pernicka*³, *Alexandra Graf*², *Elisa Bonderman*¹, *Christopher Adlbrecht*¹, *Thomas Binder*¹, *Gerald Maurer*¹, *Richard Pacher*¹, and *Julia Mascherbauer*¹

**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.
AORTIC VALVE AFFECTION IN CKD/ESRD PATIENTS
Aortic Valve Affection in CKD/ESRD Patients

• Increased calcium deposition

• The natural history of disease is different than AS in non-CKD population: accelerated progression, younger presentation.
Aortic Valve Affection in CKD/ESRD Patients

- Calcium is related to outcome
AORTIC VALVE AFFECTION IN CKD/ESRD PATIENTS

- Calcium is related to outcome
Mitral Valve Affection in CKD/ESRD Patients
Mitral Valve Affection in CKD/ESRD Patients

- Mitral annular calcification with varying severity causing regurgitation or stenosis
Mitral Valve Affection in CKD/ESRD Patients

- Embolic manifestations especially in severe forms of MAC (Caseous mitral valve calcification)
**Mitral Valve Affection in CKD/ESRD Patients**

- MAC associated with CVD morbidity and mortality
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, MPH; Joseph A. Sivak, MD; Matthew Phelan, MS; Philip J. Schultz, PhD; Utpal Patel, MD; Eric J. Velazquez, MD

JAHA 2017
**Prevalence of Left-Sided Valvular Lesions in CKD**

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

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*JAHA 2017*
PREVALENCE OF LEFT-SIDED VALVULAR LESIONS IN CKD

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

• 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

- Surgery for Aortic stenosis
- 3266 patients with moderate CKD
TREATMENT OF AORTIC STENOSIS

- TAVI/TAVR for Aortic stenosis in Germany

28,716 patients
Transcatheter or surgical aortic valve replacement in patients with advanced kidney disease: A propensity score-matched analysis

Rajkumar Doshi\textsuperscript{1}, Jay Shah\textsuperscript{2}, Vaibhav Patel\textsuperscript{1}, Varun Jauhar\textsuperscript{1}, Perwaiz Meraj\textsuperscript{1}

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAVR, n = 2485</th>
<th>TAVR, n = 2485</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>12.9</td>
<td>6.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AKI</td>
<td>50.8</td>
<td>33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dialysis requirement</td>
<td>26.8</td>
<td>20.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>49.7</td>
<td>38.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vascular complications requiring surgery</td>
<td>3.4</td>
<td>4.4</td>
<td>0.07</td>
</tr>
<tr>
<td>PPM requirement</td>
<td>9.3</td>
<td>27.8</td>
<td>&lt;0.01</td>
</tr>
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</table>

Clin Cardiol 2017
TAVI/TAVR VERSUS SURGICAL REPLACEMENT

Mortality 2.9% vs. 7.1% (p=0.09)

- Propensity score matched patients (170)

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

Am J Cardiol 2017 KDIGO
Importance of the valve durability-life 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’.

Heart 2017
Valve replacement in CKD

- 545 patients

Outcomes of cardiac surgery in chronic kidney disease

Mangalee Fernando, FRACP, Hugh S. Paterson, FRACS, Karen Byth, PhD, Benjamin M. Robinson, MBBS, MPhil, Hugh Wolfenden, FRACS, David Gracey, PhD, FRACP, and David Harris, MD, BS, FRACP

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
TAVI/TAVR IN RENAL TRANSPLANT PATIENTS

• 8 transplant patients

• All alive at 1 year

• 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**

- Due to anatomical considerations with excessive calcification, mitral valve repair often not possible.
- Similar to AVR, CKD/ESRD affects outcome after surgery.
- Repair attempted less frequently.
- Repair success equally likely.
- Repair vs. Replacement did not affect short term outcome.
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

KDIGO
Percutaneous Treatment of MR in CKD/ESRD

• 30 day mortality 25%
• 1 year mortality 53%
CHOICE OF VALVE IN ESRD PATIENTS

- 5523 mechanical valves
- 1600 tissue valves

<table>
<thead>
<tr>
<th>Studied end-point</th>
<th>Studies (N)</th>
<th>Crude incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MeV (%)</td>
<td>TiV (%)</td>
</tr>
<tr>
<td>Early mortality</td>
<td>10</td>
<td>13.9</td>
</tr>
<tr>
<td>Bleeding event</td>
<td>11</td>
<td>19.6</td>
</tr>
<tr>
<td>Re-operation</td>
<td>6</td>
<td>0.12</td>
</tr>
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</table>

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

KDIGO
**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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Patients</th>
<th>Dialysis Patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVE</td>
<td>n = 139 (%)</td>
<td>n = 139 (%)</td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td>8 (5.8)</td>
<td>26 (18.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Possible</td>
<td>4 (2.9)</td>
<td>11 (7.9)</td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>6 (4.3)</td>
<td>25 (18.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>6 (4.3)</td>
<td>23 (16.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>32 (23.0)</td>
<td>89 (64.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Ann Thoracic Surgery 2016
PROSTHETIC VALVE ENDOCARDITIS

- 38 fold increased risk of IE compared to age and gender matched population
- Increased risk among patients with no AV fistula
PROSTHETIC VALVE ENDOCARDITIS

• Predominantly Staphylococcus Endocarditis
• Mortality Predictors:
  • Age
  • DM as a cause of ESRD
  • Surgery during index hospitalization
  • Staph
  • Dysrhythmia
ORAL ANTIMICOAGULATION IN VALVULAR DISEASE
ORAL ANTIICOAGULATION IN VALVULAR DISEASE

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

• More prone for bleeding

• More options for OAC (apart from mechanical Valves)
ORAL ANTIMICROBIAL IN VALVULAR DISEASE

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

Giuseppe Andò, Piera Capranzano

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.

Int J Cardiol 2016
CONCLUSIONS I

- 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 higher mortality
  - For both surgical and interventional treatment, CKD patients show worse outcome compared to non-CKD 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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CONCLUSIONS II

• Surgical valvular replacement with tissue valves and mechanical valves show comparable outcome with less bleeding for tissue valves

• Prosthetic valve endocarditis risk is higher in ESRD, high surgical mortality

• Interventional treatment of mitral valve disease is still in the early era even von non-CKD cohorts

• Data for right sided disease are scarce
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THANK YOU

KDIGO