Update on WS 1.1, Clinical Research
Berlin,
Nov 30th - Dec 2nd

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Participants workshop S&G in cardiovascular disease

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First aim: Position paper – Gender in cardiovascular disease

To summarize S&G specific data that are relevant for patient treatment in CVD that are included in or going beyond the current European Society of Cardiology (ESC) guidelines and to identify areas of future research

Search for topics

- Aortic stenosis
- Mitral valve prolapse and regurgitation
- Coronary heart disease,
- Hypertension
- Heart Failure
  
  and its

- Pharmacological therapy
- Interventional therapy

that are relevant for patient management and should be known to treating physicians and
S&G differences in Coronary Artery Disease (CAD)

- increase in CAD in women at middle-age: more unhealthy lifestyle and obesity (diabetes)
- different manifestations of Acute Coronary Syndromes (ACS) in women:
  - sudden coronary artery dissection (SCAD): 10% ACS in women < 50 yrs
  - more type II ACS < 65 yrs (due to “functional” CAD)
  - 10x more TakoTsubo ACS (“broken heart syndrome”) in women (> 60 yrs)
  - increased 30 day and 1 year mortality in women (<65 yrs) after ACS
  - higher RF profile with more concomitant HFpEF in elderly women with CAD
- microvascular coronary disease (MCD) in 50% symptomatic women at middle-age
- male gold standard coronary angiography not suitable in women < 60 yrs.
- more co-morbidity and residual symptoms in women after PCI and/or CABG
Development Ischemic Heart Disease in women:

- **Premenopause**: Low risk
- **45-65 years**: Low-intermediate risk
- **Risk factor assessment**:
  - Functional CAD, type II ACS
  - Outward remodelling
  - Coronary microvascular disease
  - Less obstructive CAD than in men
- **Older age**: High risk

- \( \uparrow \) Obstructive CAD
- \( \downarrow \) Non-obstructive CAD
Feminine pattern of coronary artery disease:

- less stenoses coronary arteries (especially< 65 yrs)
- diffuse pattern of atherosclerosis
- less calcification, more “soft” plaques
- more (micro-)vascular dysfunction (also after PCI and CABG)
- clinical prognosis not better

♂: localized stenoses

♀: diffuse, outward atherosclerosis

Shaw LJ, et al  JACC 2009
Type 1 – coronary microvascular dysfunction (CMD)

- precursor abnormalities
- larger coronary arteries

- In 50% women with chest pain at middle-age

*courtesy P. Camici*
50% of heart failure in women is with preserved ejection fraction (HFpEF)
S&G differences in Heart Failure

- heart failure with preserved ejection fraction (HFpEF) more in **women**

- heart failure with reduced ejection fraction (HFrEF) more in **men**

- remodelling in HFpEF and HFrEF is **different** in women and men.

- hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM) more present in **men**

- TakoTsubo cardiomyopathy (TTC) and peripartum cardiomyopathy (PPCM) **women's diseases**

- in HFrEF women receive less often **cardiac resynchronisation therapy** (CRT), while they benefit more

- heart transplantation and LV assist-devices are offered at a **later stage** in women than men
Males receive most of transplanted hearts

Donor - recipient relation in heart transplantation

- men to men
- women to men
- women to women
- men to women

www.charite.de/gender
S & G differences in valvular heart disease

- Women have less calcification for same severity aortic stenosis (AoS).
- Indexation for BSA needed for correct estimation AoS.
- LV adaptation in AoS better in women.
- Prognosis AoS worse in women after surgery, but better after TAVI.
- Women with mitral insufficiency (MI) referred at later stage with worse prognosis.
- Indexation LV dimensions to body size in MI important for timing of surgery.
Gender differences in TAVI outcomes:

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Female Events/Total</th>
<th>Male Events/Total</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchanan 2011</td>
<td>279 days (median)</td>
<td>11/146</td>
<td>14/159</td>
</tr>
<tr>
<td>Hayashida 2012</td>
<td>217 days (median)</td>
<td>32/131</td>
<td>47/129</td>
</tr>
<tr>
<td>Humphries 2012</td>
<td>302 days (median)</td>
<td>57/306</td>
<td>86/278</td>
</tr>
<tr>
<td>Buja 2013</td>
<td>13 months (median)</td>
<td>59/368</td>
<td>55/291</td>
</tr>
<tr>
<td>D'Ascenzo 2013</td>
<td>490 days (mean)</td>
<td>49/216</td>
<td>50/161</td>
</tr>
<tr>
<td>Finkelstein 2013</td>
<td>480 days (median)</td>
<td>12/180</td>
<td>11/113</td>
</tr>
<tr>
<td>Al-Lamee 2013</td>
<td>475 days (median)</td>
<td>196/756</td>
<td>237/871</td>
</tr>
<tr>
<td>Diemert 2013</td>
<td>12 months</td>
<td>54/181</td>
<td>43/145</td>
</tr>
<tr>
<td>Eres 2014</td>
<td>17 months (mean)</td>
<td>11/127</td>
<td>26/97</td>
</tr>
<tr>
<td>Ferrante 2014</td>
<td>434 days (median)</td>
<td>72/348</td>
<td>82/308</td>
</tr>
<tr>
<td>Williams 2014</td>
<td>2 years</td>
<td>41/147</td>
<td>76/201</td>
</tr>
<tr>
<td>Sherif 2014</td>
<td>1 year</td>
<td>143/827</td>
<td>143/605</td>
</tr>
<tr>
<td>Total</td>
<td>737/3733</td>
<td>870/3358</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Q=19.31, DF=11 (p=0.0557); I²=43.04% (95% CI 0.00 to 71.03)
Implementation of S & G in cardiovascular disease

- governmental support
- public health: awareness programs
- standardized registration gender differences in CV care
- more multidisciplinary interaction
- more gender-specific analysis and enrollment women in clinical trials
- use appropriate trial designs and statistical tools
- improve sensitivity & specificity of symptom evaluation in women
- gender-specific data in guidelines
- implementation gender-specific strategies in clinical practice