Long-Term Outcomes Following Transcatheter Aortic Valve Implantation: Insights on Prognostic Factors and Valve Durability from the Canadian Multicenter Experience

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ACC Scientific Sessions 2012
Conflict of Interest Disclosure

 ✓ Consultant for Edwards Lifesciences, St-Jude Medical
INTRODUCTION

✓ Most data on TAVI are limited to acute and 1-year follow-up, and very few data exist on clinical outcomes and prognostic factors at longer-term follow-up

✓ Very few data exist on the long-term durability of transcatheter valves

✓ Most echo data available to date in the TAVI field:
  ✓ Single center studies or multicenter registries with no central echo core lab evaluation
  ✓ Variablity regarding the number of patients evaluated over time: no real paired evaluation of the echocardiographic exams
To evaluate the long-term outcomes following TAVI in the Multicenter Canadian Experience study, with special focus on the causes and predictors of late mortality and valve durability.
396 patients considered candidates for TAVI

5 turned down for TAVI (multicenter call conference)

339 underwent TAVI under the Canadian compassionate clinical use TAVI program

52 included in the PARTNER trial

January 2005 – June 2009

Transfemoral approach  n=167

Need for a second procedure n=6

n=1

Transfemoral Approach  n=168

Transapical approach  n=172

Transapical Approach  n=177

Cribier-Edwards (n=57)
   Edwards SAPIEN (n=275)
   SAPIEN XT (n=7)
METHODS
Clinical Follow-Up

- Clinical visits and/or phone contact at 30-days, 1-year follow-up and annually thereafter

- Follow-up available in all but 3 patients (99% of the study population)

- Median follow-up: 36 months (IQR: 26-44 months)
METHODS
Valve Durability - Echo Data

✅ Data analyzed at the Echo Core Lab of the Quebec Heart & Lung Institute directed by Dr. Philippe Pibarot and Dr. Jean Dumesnil

✅ Echo exams analyzed
  ✓ Only echos performed at the participating centers
  ✓ Only patients with serial echos over time

✅ Echo measures
  ✓ Transvalvular gradient, valve effective orifice area
  ✓ Presence, location, and severity of aortic regurgitation: multiparametric approach (ASE/EAE guidelines)
  ✓ LVEF, ventricular diameters
Baseline
339 patients

1-year follow-up
158 echocardiographic exams analyzed

- 30-day death (n=36)
- 30-day to 1-year death (n=45)
- Unsuccessful procedure, no valve implantation (n=9)
- Patient lost at follow-up (n=3)
- Echo at follow-up not performed at the participating site (n=88)

- 1- to 2-year death (n=23)
- Follow-up < 2 years (n=29)
- Echo at follow-up not performed at the participating site (n=20)

2-year follow-up
86 echocardiographic exams analyzed

- 2- to 3-year death (n=11)
- Follow-up < 3 years (n=18)
- Echo at follow-up not performed at the participating site (n=23)

3-year follow-up
34 echocardiographic exams analyzed

- Follow-up < 4 year (n=6)
- Echo at follow-up not performed at the participating site (n=17)

4-year follow-up
11 echocardiographic exams analyzed
<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n=339)</th>
<th>Transfemoral (n=162)</th>
<th>Transapical (n=177)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>81 ± 8</td>
<td>83 ± 8</td>
<td>80 ± 8</td>
<td>0.009</td>
</tr>
<tr>
<td>Male sex</td>
<td>152 (45)</td>
<td>91 (56)</td>
<td>61 (35)</td>
<td>&lt;0.0001</td>
</tr>
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<td>BMI (kg/m²)</td>
<td>26 ± 5</td>
<td>26 ± 5</td>
<td>26 ± 5</td>
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<tr>
<td>Diabetes</td>
<td>79 (23)</td>
<td>37 (23)</td>
<td>42 (24)</td>
<td>0.89</td>
</tr>
<tr>
<td>Hypertension</td>
<td>252 (74)</td>
<td>102 (63)</td>
<td>150 (85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA Functional Class</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I-II</td>
<td>29 (9)</td>
<td>11 (7)</td>
<td>18 (10)</td>
<td>0.33</td>
</tr>
<tr>
<td>III-IV</td>
<td>308 (91)</td>
<td>150 (93)</td>
<td>158 (89)</td>
<td></td>
</tr>
<tr>
<td>Chronic atrial fibrillation/flutter</td>
<td>115 (34)</td>
<td>66 (41)</td>
<td>49 (28)</td>
<td>0.01</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>234 (69)</td>
<td>110 (68)</td>
<td>124 (70)</td>
<td>0.72</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>173 (51)</td>
<td>82 (51)</td>
<td>91 (51)</td>
<td>0.91</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>99 (29)</td>
<td>47 (29)</td>
<td>52 (30)</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior coronary artery bypass grafting</td>
<td>116 (34)</td>
<td>49 (30)</td>
<td>67 (38)</td>
<td>0.17</td>
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</table>
### Baseline Characteristics (2)

<table>
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<tr>
<th>Variable</th>
<th>All patients (n=339)</th>
<th>Transfemoral (n=162)</th>
<th>Transapical (n=177)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
<td>77 (23)</td>
<td>27 (17)</td>
<td>50 (29)</td>
<td>0.01</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>120 (35)</td>
<td>31 (19)</td>
<td>89 (50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>100 (30)</td>
<td>45 (28)</td>
<td>55 (31)</td>
<td>0.55</td>
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<tr>
<td>Creatinine (umol/l)</td>
<td>119 ± 83</td>
<td>124 ± 85</td>
<td>113 ± 81</td>
<td>0.23</td>
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<tr>
<td>eGFR&lt;60ml/min</td>
<td>191 (56)</td>
<td>86 (53)</td>
<td>104 (59)</td>
<td>0.33</td>
</tr>
<tr>
<td>STS score (%)</td>
<td>9.8 ± 6.4</td>
<td>9.0 ± 5.8</td>
<td>10.5 ± 6.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>61 (18)</td>
<td>28 (17)</td>
<td>33 (19)</td>
<td>0.78</td>
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<tr>
<td>Frailty</td>
<td>85 (25)</td>
<td>42 (26)</td>
<td>43 (24)</td>
<td>0.80</td>
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<tr>
<td>Pulmonary hypertension</td>
<td>84 (25)</td>
<td>35 (22)</td>
<td>49 (28)</td>
<td>0.26</td>
</tr>
<tr>
<td>Severe Mitral Regurgitation</td>
<td>27 (8)</td>
<td>18 (11)</td>
<td>9 (5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean Aortic Gradient (mmHg)</td>
<td>46 ± 17</td>
<td>48 ± 18</td>
<td>44 ± 17</td>
<td>0.08</td>
</tr>
<tr>
<td>Aortic Valve Area (cm²)</td>
<td>0.63±0.17</td>
<td>0.63 ± 0.16</td>
<td>0.63±0.18</td>
<td>0.93</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>55 ± 14</td>
<td>55 ± 14</td>
<td>56 ± 14</td>
<td>0.72</td>
</tr>
<tr>
<td>LVEF&lt;40</td>
<td>54 (16)</td>
<td>26 (16)</td>
<td>28 (16)</td>
<td>1.00</td>
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</tbody>
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## Procedural and 30-Day Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Procedures (n=345)</th>
<th>Transfemoral (n=168)</th>
<th>Transapical (n=177)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td><strong>Procedural variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Successful procedure</td>
<td>322 (93.3)</td>
<td>152 (90.5)</td>
<td>170 (96.0)</td>
<td>0.051</td>
</tr>
<tr>
<td>Procedural death</td>
<td>6 (1.7)</td>
<td>3 (1.8)</td>
<td>3 (1.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Valve embolization</td>
<td>7 (2.0)</td>
<td>5 (3.0)</td>
<td>2 (1.1)</td>
<td>0.27</td>
</tr>
<tr>
<td>Need for a second valve</td>
<td>9 (2.6)</td>
<td>4 (2.4)</td>
<td>5 (2.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Conversion to open heart surgery</td>
<td>6 (1.7)</td>
<td>2 (1.2)</td>
<td>4 (2.3)</td>
<td>0.69</td>
</tr>
<tr>
<td>Need for hemodynamic support</td>
<td>14 (4.1)</td>
<td>7 (4.2)</td>
<td>7 (4.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Major access site complications</td>
<td>45 (13.0)</td>
<td>22 (13.1)</td>
<td>23 (13.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Life threatening arrhythmias</td>
<td>28 (8.1)</td>
<td>12 (7.1)</td>
<td>16 (9.0)</td>
<td>0.56</td>
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<tr>
<td><strong>30-day outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>4 (1.2)</td>
<td>1 (0.6)</td>
<td>3 (1.7)</td>
<td>0.62</td>
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<tr>
<td>Stroke</td>
<td>8 (2.3)</td>
<td>5 (3.0)</td>
<td>3 (1.7)</td>
<td>0.49</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10 (2.9)</td>
<td>5 (3.0)</td>
<td>5 (2.8)</td>
<td>1.00</td>
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<tr>
<td>Need for hemodialysis</td>
<td>9 (2.6)</td>
<td>3 (1.8)</td>
<td>6 (3.4)</td>
<td>0.50</td>
</tr>
<tr>
<td>Need for pacemaker</td>
<td>17 (4.9)</td>
<td>6 (3.6)</td>
<td>11 (6.2)</td>
<td>0.32</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>36 (10.4)</td>
<td>16 (9.5)</td>
<td>20 (11.3)</td>
<td>0.73</td>
</tr>
</tbody>
</table>
Predictive Factors of 30-day Mortality

- **Pulmonary Hypertension**: OR: 2.09, 95% CI: 1.02-4.33, P=0.048
- **Severe Mitral Regurgitation**: OR: 3.01, 95% CI: 1.09-8.24, P=0.033
- **Need for peri-procedural hemodynamic support**: OR: 6.84, 95% CI: 2.04-22.93, P=0.002
CAUSES OF DEATH AT FOLLOW-UP
Multicenter Canadian Experience

Non cardiac (n=74)
Cardiac (n=29)
Unknown (n=7)
CAUSES OF NON-CARDIAC DEATH AT FOLLOW-UP Multicenter Canadian Experience

- Pulmonary (n=36) 13.5%
- Renal failure (n=11) 48.6%
- Stroke (n=6) 8.1%
- Major bleeding (n=6) 8.1%
- Cancer (n=5) 14.9%
- Other (n=10) 6.8%
# Predictive Factors of Late (＞30 days) Mortality

<table>
<thead>
<tr>
<th>Condition</th>
<th>Late Mortality</th>
<th>Hazard Ratio</th>
<th>95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic obstructive pulmonary disease</strong></td>
<td>Yes (n=110)</td>
<td>42 (38.5%)</td>
<td>1.99</td>
<td>1.34-2.95</td>
</tr>
<tr>
<td></td>
<td>No (n=190)</td>
<td>44 (23.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic kidney disease</strong></td>
<td>Yes (n=110)</td>
<td>67 (60.9%)</td>
<td>1.62</td>
<td>1.09-2.41</td>
</tr>
<tr>
<td></td>
<td>No (n=190)</td>
<td>96 (50.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic atrial fibrillation</strong></td>
<td>Yes (n=110)</td>
<td>47 (43.1%)</td>
<td>1.82</td>
<td>1.24-2.67</td>
</tr>
<tr>
<td></td>
<td>No (n=190)</td>
<td>54 (28.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Frailty</strong></td>
<td>Yes (n=110)</td>
<td>35 (31.8%)</td>
<td>1.76</td>
<td>1.17-2.64</td>
</tr>
<tr>
<td></td>
<td>No (n=190)</td>
<td>42 (22.1%)</td>
<td></td>
<td></td>
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</table>
### 48-month Follow-Up Survival Curves / Freedom from Cardiac Death

**Canadian Multicenter Experience**

#### Patients at risk:

<table>
<thead>
<tr>
<th>Patients at risk:</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
<th>42</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>339</td>
<td>271</td>
<td>248</td>
<td>221</td>
<td>190</td>
<td>141</td>
<td>92</td>
<td>59</td>
<td>31</td>
</tr>
<tr>
<td>Transfemoral</td>
<td>162</td>
<td>132</td>
<td>119</td>
<td>107</td>
<td>96</td>
<td>72</td>
<td>50</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>Transapical</td>
<td>177</td>
<td>140</td>
<td>134</td>
<td>113</td>
<td>93</td>
<td>68</td>
<td>41</td>
<td>25</td>
<td>14</td>
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</table>

#### Months follow-up

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
<th>42</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free of cardiac death (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients (n=339)</td>
<td>85%</td>
<td>87%</td>
<td>85%</td>
<td>83%</td>
<td>78%</td>
<td>78%</td>
<td>78%</td>
<td>76%</td>
<td>75%</td>
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<tr>
<td>Transfemoral (n=162)</td>
<td>84%</td>
<td>86%</td>
<td>80%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>Transapical (n=177)</td>
<td>87%</td>
<td>86%</td>
<td>80%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
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</tbody>
</table>
CAUSES OF CARDIAC DEATH AT FOLLOW-UP
Multicenter Canadian Experience

- Cardiac failure (n=19) - 65.6%
- Sudden death (n=4) - 13.8%
- Myocardial infarction (n=4) - 13.8%
- Endocarditis (n=1) - 3.4%
- Post-mitral replacement (n=1) - 3.4%

No cases of structural valve failure during the follow-up period.
# Predictive factors of cumulative cardiac mortality at follow-up

<table>
<thead>
<tr>
<th>Cumulative Cardiac Mortality</th>
<th>Yes (n=65)</th>
<th>No (n=274)</th>
<th>Hazard Ratio</th>
<th>95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary hypertension</td>
<td>23 (35.4%)</td>
<td>61 (22.3%)</td>
<td>1.92</td>
<td>1.15-3.23</td>
<td>0.013</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>47 (72.3%)</td>
<td>143 (52.2%)</td>
<td>2.30</td>
<td>1.31-4.03</td>
<td>0.003</td>
</tr>
</tbody>
</table>
48-month Follow-Up Survival Curves / Freedom from Stroke Canadian Multicenter Experience

Free of stroke (%)

- All patients (n=339)
- Transapical (n=177)
- Transfemoral (n=162)

Patients at risk:
- All patients: 339, 260, 236, 211, 177, 122, 78, 50, 26
- Transapical: 177, 133, 124, 108, 84, 54, 32, 20, 11
- Transfemoral: 162, 126, 111, 102, 92, 68, 45, 29, 14
48-month Follow-Up Survival Curves / Freedom from Death and Stroke
Canadian Multicenter Experience

**Patients at risk:**

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Transfemoral</th>
<th>Transapical</th>
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<tbody>
<tr>
<td>Patients at risk</td>
<td>339</td>
<td>162</td>
<td>177</td>
</tr>
</tbody>
</table>

**Free of death and stroke (%):**

- All patients (n=339)
  - Transfemoral (n=162)
  - Transapical (n=177)

<table>
<thead>
<tr>
<th>Months follow-up</th>
<th>All patients</th>
<th>Transfemoral</th>
<th>Transapical</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>90</td>
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<tr>
<td>12</td>
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<td>36</td>
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<tr>
<td>42</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>48</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

Months follow-up:

- 6 months: 73%
- 12 months: 72%
- 18 months: 74%

Freedom from death and stroke (%) at 36 months:

- All patients: 48%
- Transfemoral: 47%
- Transapical: 49%

Freedom from death and stroke (%) at 48 months:

- All patients: 45%
- Transfemoral: 47%
- Transapical: 44%
Functional status / NYHA CLASS

Baseline

Last follow-up

% of patients

p < 0.0001

Baseline

Last follow-up

NYHA class

IV

III

II

I

0.8

11.6

36.7

50.9

69.1

7.4

1.2

22.3
Mean Gradient and Aortic Valve Area Over Time

A. n=158

B. n=86

C. n=34

D. n=11
Mean Gradient and Aortic Valve Area Over Time (Edwards SAPIEN valve)

A

n=137

B

n=76

C

n=31

D

n=7
Aortic Regurgitation Over Time

A

n=158

% of patients

Baseline Discharge 1Y

p=0.662

B

n=86

% of patients

Baseline Discharge 1Y 2Y

p=0.669

C

n=34

% of patients

Baseline Discharge 1Y 2Y 3Y

p=0.951

D

n=11

% of patients

Baseline Discharge 1Y 2Y 3Y 4Y

p=0.937

Degree of Aortic Regurgitation

- Severe
- Moderate
- Mild
- None/Trace
Aortic Regurgitation Over Time (Edwards SAPIEN valve)

A

\[ n=137 \]

\[
\begin{array}{ccc}
\text{% of patients} & \text{Baseline} & \text{Discharge} & \text{1Y} \\
\hline
0 & 20 & 40 & 100 \\
\end{array}
\]

\[ p=0.616 \]

B

\[ n=76 \]

\[
\begin{array}{ccc}
\text{% of patients} & \text{Baseline} & \text{Discharge} & \text{1Y} & \text{2Y} \\
\hline
0 & 20 & 40 & 100 \\
\end{array}
\]

\[ p=0.680 \]

C

\[ n=31 \]

\[
\begin{array}{ccc}
\text{% of patients} & \text{Baseline} & \text{Discharge} & \text{1Y} & \text{2Y} \\
\hline
0 & 20 & 40 & 100 \\
\end{array}
\]

\[ p=0.992 \]

D

\[ n=7 \]

\[
\begin{array}{ccc}
\text{% of patients} & \text{Baseline} & \text{Discharge} & \text{1Y} & \text{2Y} & \text{3Y} & \text{4Y} \\
\hline
0 & 20 & 40 & 100 \\
\end{array}
\]

\[ p=0.896 \]

Degree of Aortic Regurgitation:
- Severe
- Moderate
- Mild
- None/Trace
Aortic Regurgitation Type: Paravalvular / Transvalvular

- Discharge: n=158, p=0.429
- 1Y: n=86, p=0.391
- 2Y: n=34, p=0.144
- 3Y: n=11, p=0.278

Aortic Regurgitation Type:
- Both
- Transvalvular
- Paravalvular
Mild Aortic Regurgitation and LV Changes Over Time

A

B

C

D

E

F

- LVED (mm)
- LVF (%)

- Mild
- None/Trace

- Baseline
- Discharge
- 1Y
- 2Y

p-values for comparing groups:

A: p=0.648
B: p=0.583
C: p=0.897
D: p=0.708
E: p=0.824
F: p=0.650

p=0.630 between groups
p=0.843 between groups
p=0.242 between groups
p=0.977 between groups
p=0.314 between groups
p=0.897 between groups
CONCLUSIONS
Canadian Multicenter Experience / Long-Term Results

✓ A multicenter TAVI program with a balloon-expandable valve including non-operable or very high risk patients was associated with a survival rate of 57% after a median follow-up of 3 years, with no differences between TF and TA approaches.

✓ Two thirds of late deaths were of non-cardiac origin and were mostly determined by a history of COPD, CKD, chronic atrial fibrillation and frailty.

✓ About 1/3 of late deaths were of cardiac origin, mostly secondary to cardiac failure. Pulmonary hypertension determined a higher rate of periprocedural death and remained a predictor of cardiac death at follow-up.
CONCLUSIONS
Canadian Multicenter Experience / Long-Term Results

- Valve function remained stable up to 4-year follow-up, with only mild non-significant changes in transvalvular gradient and valve area.

- No significant changes were observed over time in the presence and degree of residual aortic regurgitation.

- Mild aortic regurgitation (mostly paravalvular) was frequent after TAVI, but had no impact on LV diameters and function.