Impact of obesity on sepsis outcomes

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Disclosure / Conflict of Interest

• No Conflict of Interest with respect to this presentation.
Severe Sepsis
All hospitalized
Half ICU

Obesity Paradox

• Critically ill obese patients have better outcomes despite:
  – Diabetes
  – Respiratory dysfunction
  – Chronic inflammatory state

• Is this true in sepsis?
• Is the inflammatory response different?
• Relationship to lipoprotein levels, cytokines?
Critically ill obese patients: meta-analysis

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>obese n/N</th>
<th>Nonobese n/N</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marik P</td>
<td>1724/12011</td>
<td>6509/36165</td>
<td></td>
</tr>
<tr>
<td>El-Solh A</td>
<td>35/117</td>
<td>22/132</td>
<td></td>
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<tr>
<td>Garrouste Orgeas M</td>
<td>57/227</td>
<td>475/1471</td>
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<td>O'Brien JM</td>
<td>137/457</td>
<td>413/1031</td>
<td></td>
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<tr>
<td>Ray D E</td>
<td>57/550</td>
<td>237/1598</td>
<td></td>
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<tr>
<td>Aldawood</td>
<td>134/540</td>
<td>394/1295</td>
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<td>Bochicchio G</td>
<td>13/62</td>
<td>166/1105</td>
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<tr>
<td>Nasraway S</td>
<td>22/366</td>
<td>87/1007</td>
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</tr>
<tr>
<td>Peake SL</td>
<td>26/129</td>
<td>69/304</td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>14459</td>
<td>44108</td>
<td></td>
</tr>
<tr>
<td>Total events:</td>
<td></td>
<td></td>
<td>2205 (obese), 8372 (Nonobese)</td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 18.35, df = 8 (P = 0.02), I² = 56.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.33 (P = 0.0009)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

60-Day In-Hospital Mortality (ICON ICU patients n=8829)

Sakr et al. Crit Care Med. 2015
Septic shock: VASST

- creatinine: 191-130 µmol/L
- female: 45-38%
- fluid/kg: 130-180 mL/kg
- pressor/kg: NE 0.13-0.26
- pneumonia: 35-50%
- fungal: 8.2-15.6%

<table>
<thead>
<tr>
<th>Number at Risk</th>
<th>Days</th>
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</thead>
<tbody>
<tr>
<td>BMI &gt;30 kg/m²</td>
<td>245</td>
</tr>
<tr>
<td>BMI 25-29.9 kg/m²</td>
<td>209</td>
</tr>
<tr>
<td>BMI &lt;25 kg/m²</td>
<td>276</td>
</tr>
</tbody>
</table>
Cytokine inflammatory response
VAT may be “bad” fat

VAT/SAT
Visceral Adipose Tissue / Subcutaneous Adipose Tissue
High VAT/SAT is bad

P<0.005

Number at Risk

<table>
<thead>
<tr>
<th>Quartile</th>
<th>64</th>
<th>61</th>
<th>57</th>
<th>56</th>
<th>54</th>
<th>53</th>
<th>52</th>
<th>51</th>
<th>50</th>
<th>50</th>
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<tbody>
<tr>
<td>Quartile 1</td>
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<td>53</td>
<td>49</td>
<td>47</td>
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<td>41</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>64</td>
<td>57</td>
<td>49</td>
<td>43</td>
<td>41</td>
<td>38</td>
<td>37</td>
<td>36</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>Quartile 3</td>
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<td>56</td>
<td>41</td>
<td>39</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>31</td>
<td>31</td>
<td>31</td>
</tr>
</tbody>
</table>

P=0.028 at day 28

P=0.005 at day 90
90-day mortality by VAT/SAT

P=0.004

P=0.023

Pro/anti-inflammatory ratio: IL8 / IL10

\[ P = 0.043 \]
VAT/SAT related to LDL

Survival

Days

P = 0.043

LDL

Low VAT/SAT  High VAT/SAT

P = 0.006
Low LDL, HDL levels in sepsis

Low LDL, HDL are bad

At-risk patients:

<table>
<thead>
<tr>
<th>HDL &gt; 25.1mg/dL</th>
<th>132</th>
<th>131</th>
<th>130</th>
<th>125</th>
<th>124</th>
<th>123</th>
<th>121</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL &lt; 25.1mg/dL</td>
<td>68</td>
<td>62</td>
<td>57</td>
<td>54</td>
<td>52</td>
<td>52</td>
<td>51</td>
</tr>
</tbody>
</table>
VAT/SAT related to LDL

![Graph showing survival days and LDL levels with low and high VAT/SAT](image)

- Low VAT/SAT
- High VAT/SAT

**P = 0.043**

**P = 0.006**
Conclusions

• Obesity paradox particularly strong in sepsis
  – High BMI protects against mortality?

• Low VAT/SAT is beneficial at any BMI

• Is SAT good?
  – Not as pro-inflammatory as VAT?
  – Protects against lipoprotein drop?
  – Sequesters pathogen lipids?
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Harvey Coxson
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Chawika Pisitsak
Bandarn Suetrong
Kelly Genga
Joseph Lee

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