The Haematological Malignancy Patient on the Intensive Care Unit

SODIT

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Dr Bryson Pottinger, Consultant Haematologist
Royal Cornwall Hospital
Overview

• The usual story
• What the Haematologist is up against
• Historical outcomes
• Improvements in outcome
• Trial by ICU
• Recommendations
What We Say

• “They’re ‘different’ from other ICU patients”
• “They’re young, we made them ill, so you need to do something”
• “We’ve cured their malignancy, all you need to do is get them over this acute illness”
• “Don’t worry, the neutrophil count will recover in 2-3 days”
• “Can we change that anti-fungal/antibiotic?”
• “In fact, can we add a few more?”
What You Say

• “Patients with leukaemia/lymphoma/stem cell transplant (delete as applicable) just come to ICU to die”
• “I’ll come & have a look, but there’s not much point – they all die anyway”
• “They can’t survive with no white cells”
• “Their leukaemia is too bad”
What I Have to Consider - AML

AML 10,12: Survival from CR by risk group
Poor risk

<table>
<thead>
<tr>
<th></th>
<th>No transplant</th>
<th>Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Patients</td>
<td>143</td>
<td>64</td>
</tr>
<tr>
<td>Obs.</td>
<td>68</td>
<td>40</td>
</tr>
<tr>
<td>Exp.</td>
<td>56.0</td>
<td>52.0</td>
</tr>
</tbody>
</table>

2P = 0.01
33%
18%
What I Have to Consider - ALL

Overall Survival

Percent

Years

n=1913

39%
What I Have to Consider - DLBCL NHL
What I Have to Consider - BL NHL
Do They All Die? Historical Evidence – 80s

- 1988: 13 out of 60 (21%) patients survived to hospital discharge. Higher mortality than other patient groups
  Lloyd-Thomas et al *BMJ* 296: 1025 – 1029

- 1989: Only 1 of 40 patients with progressive pneumonia survived
  Denardo *Crit Care Med* 17(1): 4-6
Do They All Die? Historical Evidence – 90s

• 1993: BMT patients – only 1 of 28 patients ventilated survived ICU
  Paz et al Chest 104:527 – 531

• 1995: “AML patients who require ventilatory support for acute respiratory failure rarely survive their ICU admission”

• 1996: BMT centre in Seattle – “of the patients who required mechanical ventilation, no-one survived with lung injury combined with haemodynamic instability, hepatic failure or renal failure”
  Rubenfeld et al Annals Int Med 125(8): 625-633
Do They All Die?-Historical Evidence 80s and 90s

- 2005: Retrospective study from Australia over 10 year period (1989-1999)
- Improved mortality over time (1\textsuperscript{st} vs 2\textsuperscript{nd} 5 year period)

Do They All Die? - Historical Evidence 80s and 90s

Rubenfeld et al  *Annals Int Med* 125(8): 625-633
What About The 21st Century?

- 2004: German study – AML & pulmonary infiltrates requiring invasive ventilation
  - 87% died (26/30)
  - 4/10 survived <50 yrs old
  - 0/20 if >50 years old
- No difference for APACHEII, LFTs, BUN, AML prognostic factors
- But “prolonged ventilation does not preclude survival”

Rabe et al *Journal Critical Care* 19(1):29-35
What About The 21st Century?

- French retrospective study (n=83) in AML patients
- 60% were neutropenic on admission
- Mechanical ventilation in 57%
- ICU mortality 34%
- 49% of ICU survivors died within 1 year of ICU discharge
- ICU mortality rate ≈
  - simplified acute physiology score II
  - IMV
- 1 year survival ≈
  - haematological prognostic factors (AML M3 or CR)
  - age, performance status
- ICU admission justified for selected patients with AML

Rabbat et al Brit Journal Haem 2005; vol 129: 350-357
What About The 21\textsuperscript{st} Century?

- 2005: Dutch study
  - ICU outcome predicted by sequential organ failure assessment (SOFA) scores.
    

- 2002: French study
  - Severity of the underlying hematologic malignancy does not influence intensive care unit or hospital mortality.
  - Short-term prognosis is exclusively predicted by acute organ dysfunctions and by pathogen (fungus)
  - “reluctance to admit patients with non-terminal hematologic malignancies to the intensive care unit based only on the prognosis of their underlying hematologic malignancy does not seem justified.”

What About The 21st Century?

Figure 2 Thirty-day mortality rates (% y axis) by number of organ failures (columns)

<table>
<thead>
<tr>
<th>Number of Organ Failures</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
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<tr>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>
What About The 21st Century?

- 2008: 90 acute leukaemia patients admitted 2001-2004
  - 68% needed ventilatory support
  - 27% patients survived to be discharged from hospital & were alive 2 months later
  - APACHEII, use of pressors, BMT, adverse cytogenetics predicted worse outcome.
  - Newly diagnosed leukaemia and type did not
  - A diagnosis of acute leukaemia should not disqualify patients from an ICU admission

Thakkar et al. *Cancer* 112 (10): 2233-2240
What About The 21st Century?

- 2009: Critically ill cancer patients – 3147 patients from 198 ICUs in 24 European countries
- ICU mortality rates
  - No cancer – 23%
  - Solid tumours – 27%
  - Haematological malignancies – 58%
- “Patients with cancer on the ICU: the times they are changing”

Taccone et al Critical Care 13(1):R15
What About The 21st Century?

- 2009: ICNARC data – 7689 admissions
  - Admissions with haematological malignancies to 178 UK ICUs
  - 1995 – 2007
  - 7689 admissions
  - ICU mortality 43%
  - Acute hospital mortality 59%
    Hampshire et al *Critical Care* 2009: vol 13: R137

- 2012: Marsden data – specialist cancer ICU
  - 52% required mechanical ventilation
  - ICU mortality 34%
  - Hospital mortality 46% (assoc with MV & ≥2 organ failures)
  - Neutropenia, transplant status and APACHEII not predictive
    Bird et al *Brit Jounal Anaesthesia* 108(3):452-9
What About The 21st Century?

- 714 haematological malignancy patients admitted to Scottish ITUs
- ICU mortality 39%, hospital mortality 55%
- Predictors of poor outcome
  - CPR before admission
  - Inotropic support in the first 24 hrs
  - APACHEII score
  - Ventilatory support on admission
- Neutropenia not independent predictor

Cuthbertson, BH. JICS Vol 9, No 2 July 2008
What About The 21\textsuperscript{st} Century?

- Birmingham Heartlands 2004-2011
- 50 consecutive ITU admissions with haematological malignancy
  mortality 91\% (2004-2007)
  mortality 36\% (2008-2011)

Lewis H, Critical care 2012, 16(suppl 1):P409
Effect of ICU Experience on Outcome

• No of patients with haematological malignancy & acute respiratory failure admitted to ICU per year
  – Low - <12 per year
  – Intermediate 12-30 per year
  – High>30 per year
• Patients in high volume ICUs had lower mortality than other patients

Lecuyer et al *Eur Resp Jour* 2008: 32: 748 - 754
Trial Of ICU Trial

- Prospective study
- ICU trial - full treatment for 4 days – re-appraisal day 5
- Criteria
  - Not meeting automatic ICU admission criteria
  - Remission or stable disease with scheduled intensification
  - Prognosis unclear / not yet assessable
  - Availability of potentially lifespan-extending cancer treatment
  - No allogeneic transplants (or HIV positive)
  - ≥ 1 other organ failure
- Patients
  - 114 non-trial (full code) vs.
  - 188 given ICU trial – 85 died ≤5 days, 103 survived 1st 4 days

Trial Of ICU Trial

All cancer patients for whom ICU admission was requested

1. Bedridden patients
2. Palliative care the only cancer treatment option
3. Patient refuses ICU admission

- No ICU admission
  - Comfort and palliative care

- ICU admission for an ICU Trial

1. Previously untreated malignancy
2. Acute tumor lysis syndrome
3. Bulky or infiltrating tumors at the earliest phase of treatment
4. Patients in complete remission

- ICU admission for full care management including unlimited lifesustaining interventions

Trial Of ICU Trial

- Results:
  - 32% mortality in full code cohort
  - 79% mortality in trial cohort (60% in those surviving to day 5)
  - Linear relation on day 6 of number of organ failures & mortality

- Day 6 figures:
  - 26% - 1 organ; 55% 2 organ failures, 85% with 5 organ failures

- From day 3 onwards, organ dysfunction score worse in non-survivors than in survivors

- All patients that required initiation of MV, vasopressors or dialysis after 3 days in the ICU died

- No difference in malignancy characteristics
Figure 3. Changes in the Logistic Organ Dysfunction Score throughout the intensive care unit stay in survivors (open triangles) and nonsurvivors (filled circles).
Figure 4. Time from intensive care unit admission to initiation of mechanical ventilation, vasopressors, and renal replacement therapy in patients who survived 5 days. Each subject is depicted separately. Open triangles, survivors; closed circles, nonsurvivors.
Knowing When to Quit

- Dutch study from 2011
  - 86 patients including allo-transplant patients
  - Organ dysfunction scores (APACHE-II, SOFA) at ICU admission & days 1, 3, 5 & 7
  - Prognostic factors
    - Need for MV or inotropes
    - Deceasing SOFA score – better prognosis than if unchanged or increasing
      - “Unchanged or increasing SOFA scores still out-perform all other parameters as markers of an unfavourable prognosis.”
    - “Unlimited treatment for a limited amount of time”
  
Early Referral to ICU/Outreach

- Improving pre-ICU care
  - Early warning scores
  - Access to senior clinicians
  - Early goal-directed therapy
  - Care bundles eg “Surviving Sepsis” campaign

- French study – outcome of cancer patients considered for ICU
  - 26% “too sick” – but 17% alive at day 180
  - 23% “too well” – but only 79% alive at 30 days
  - Need for a broader admission policy

Thiéry et al 2005 *JCO* 23: 4406-4413
Recommendations

• Close collaboration between intensivists & haematologists
• Management discussions “in the cold light of day” often at MDT
• Early ICU involvement – outreach
• Realistic outcome expectations
• Regular review on ICU by haematology team
• Who does what, to whom & when
• Prepare to withdraw active support (≥ Day 5+)
• Morbidity & mortality meetings to include ICU admissions
Discussion