温乳器及び内容器の消毒、乾燥は1日1回とする

＜研究1＞温乳器消毒方法の変更による器具およびミルクからの緑膿菌検出の推移

2004年4月以降従来の方法から温乳器消毒法を変更し、温乳器具およびミルクからの緑膿菌検出の推移を検討した。

（方法）

温乳器、内容器、母乳（6名分)、13%普通ミルク（1本）につき細菌培養検査を行った。尚、母乳・ミルクについては以下のように経時的に細菌培養検査を行った。

母乳ー解凍直後、温乳開始後1時間、（2時間)、3時間、3.5時間

ミルクー温乳開始後1時間、3時間、3.5時間

C. 研究結果

研究1の結果

1 従来の方法では、24時間使用後の温乳器の底、排水ホース、温水の全てから *P. aeruginosa* が検出された。

2 変更後の方法(1)では、温乳器の底に *P. aeruginosa* が微少、内容器の温水にStaphylococcus sp が数コロニー検出されたが、他の箇所は培養陰性であった。また、ミルクは3.5時間経過しても細菌は検出されなかった。母乳は3時間にて全てにおいて許容範囲内であるが、Staphylococcus sp が＜1×$10^5$ GFU／ml 検出された。

3 変更後の方法(2)では、器具およびミルク・母乳の3時間経過後も含めて、細菌培養検査の全てが陰性であった。

＜研究2＞温乳器消毒方法変更前後におけるNICU緑膿菌保菌者および感染症発症者の推移

（方法）2001年1月から2004年12月までの月平均のNICU入院者数、緑膿菌保菌者数、緑膿菌保菌者率、感染症発症者数を調査した。

研究2の結果

結果を表1に示す。

2004年4月以降に温乳器消毒方法を変更後、月平均のNICU入院者数は変わらなかったが、緑膿菌保菌者数および緑膿菌保菌者率は有意に減少し、2004年4月以降の緑膿菌感染症の発症者はなくなった。

D. 考察

*P. aerginosa* は乾燥に弱く、湿った所に繁殖しやすい特徴があり、本来は温水を使用しないことが最適である。温水を使用しない保温庫の使用も考慮したが、ミルクの量や哺乳瓶の配置で温まり方の差がでてくるという報告もあり、当NICUでは不適切と判断した。そこで、従来の1台の温乳器を使用しながら消毒回数を増やす→温乳器の中に内容器を用い、温乳毎に毎回新しい温水を交換する→温乳器・内容器をもう1台ずつ購入し、毎日交互に使用し消毒後24時間乾燥させる、など方法を変更した。

その結果ミルク・母乳に関しては、解凍直後から母乳の細菌数が温乳時間に関係なく、細菌の検出はなくなった。

温乳器に関しては、変更前には温乳器の全ての場所より *P. aeruginosa* が検出されたが、変更後の方法(1)では温乳器の底のみ *P. aeruginosa* が微少と著しく減少し、方法(2)では検出しなくなった。それに伴って、NICUにおける緑膿菌保菌者数（率）が低下し、感染症発症者も減少した。従って、従来の方法では乳首や哺乳瓶周囲に付着した温水が、感染経路になっていた可能性が考えられた。

NICU内の環境の細菌サーベイランスでも、手洗い場所などの水周りには時に *P. aeruginosa* が検出される。恒温槽を持つ温乳器は細菌の繁殖には好条件であり、多くの細菌の繁殖を促すリスクがあることを念頭に管理すべきと思われる。

E. 結論

温乳器の消毒方法および温乳方法を変更する

ことにより、NICU 内の緑膿菌保菌者・感染症発症者が減少した。緑膿菌感染症に関しては、環境のあらゆる水周りが感染源になりうることを考慮すべきである。

G. 研究発表

論文発表

なし

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表 1　温乳器消毒方法変更前後における NICU 緑膿菌保菌者および感染症発症者の推移

| | NICU 入院者数 (人/月) | 緑膿菌保菌者数 (人/月) | 緑膿菌保菌者率 (%) | 感染症発症者数 (人) |
|---|---|---|---|---|
| 2001.1～12 | 32.5 | 3.92 | 12.1 | 2 |
| 2002.1～12 | 35.1 | 3.17 | 9.0 | 1 |
| 2003.1～12 | 35.7 | 4.83 | 13.5 | 4 |
| 2004.1～3 | 37.3 | 6.33 | 17.0 | 1 |
| 2004.4～12 | 34.6 | 1.44 | 4.2 | 0 |

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分担研究報告書

# 超早産児の真菌感染に対するフルコナゾール予防投与の効果に関する研究

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研究要旨：超早産児における真菌感染症の合併は予後に影響する問題であり、治療に難渋することが多いため予防的管理が望まれる。2002 年からフルコナゾール(FLCZ)の予防的投与を開始し、その有効性と副作用の有無について比較した。在胎 27 週未満の児で、FLCZ を予防投与した 13 例と予防投与を行わなかった 19 例を対象とした。FLCZ の予防投与法は 3mg/kg を出生時から 2 日おきに経腸栄養が確立するまで静脈内投与した。真菌感染と消化管病変合併例は予防投与なし群の 7 例(37%) と 8 例(42%)から、予防投与あり群の 0 例(0%)と 1 例(8%)に有意に減少していた。副作用と思われる症状と検査値異常は認めなかった。FLCZ 予防投与は超早産児の予後を改善させる有効な対策となりうると考えられた。

研究協力者：大城　誠　大垣市民病院第二小児科（小児循環器・新生児科）医長

## A. 研究目的

超低出生体重児の管理においては、真菌感染症の合併は予後を左右する重篤な問題である。真菌感染症は治療に難渋することが多いため、その予防に努める周産期管理が望まれる中で、Kaufman らが超低出生体重児に対してフルコナゾール(FLCZ)を生後 6 週間予防投与することにより、副作用なく真菌感染および保菌率を有意に低下させることを報告した。

大垣市民病院 NICU では 2000 年頃から超早産児においてカンジダ感染症の合併が増加し、比較的早期から治療を開始していたにも関わらず、死亡例も認められた。そこで Kaufman らの方法に準じて、2002 年 4 月から在胎 27 週未満の超早産児に限定して FLCZ を予防投与する対策をとった。その成果について後方視的に検討し、その有効性と副作用の有無について検討した。

## B. 研究方法

2000 年 1 月～2004 年 3 月までに入院した在胎 27 週未満の超早産児は 38 例であり、胎児水腫にて死亡した 1 例と先天性心疾患を合併した 2 例を除外した。2002 年 4 月から FLCZ の予防投与を開始したが、投与を受けなかった 3 例を除いた 13 例（予防投与有り群）と、対照として予防投与開始以前の 19 例（予防投与なし群）を比較検討した。

FLCZ は 3 mg/kg/day の投与量を生後 2 週間以内は日齢 0 から 2 日おきに、生後 2 週間以降は 1、2 日おきを基本として点滴静注した。投与中止基準は経腸栄養が十分に確立し、中心静脈ラインを用いた輸液が中止できるまでとし、主治医が判断した。

真菌感染は抗生剤に反応のない感染兆候に加え、真菌培養結果が陽性で、β-D-グルカン値の上昇を参考に最終的に診断した。真菌感染とは判断されずに真菌が検出された場合を保菌例とし、感染例と合わせて真菌検出例とした。

予防投与前後の対象児について出生前後の臨床因子、急性期管理方法を比較し、真菌感染合併率と真菌検出率、真菌以外の感染症合併率、死亡率、NICU 退院時までの合併症（症候性動脈管開存症、頭蓋内出血、消化管病変、慢性肺疾患、未熟児網膜症）の有無を検討した。FLCZ の副作用として臨床症状の他に、生後 1 ヶ月未満での白血球増加（白血球数 20,000/μL 以上）、白血球減少（白血球数 5,000 /μL 未満）、肝機能障害、腎機能障害（血清クレアチニン 1.5 mg/dL 以上）の有無について検討した。

倫理面への配慮

本研究は、通常の臨床検査にて得られたデータを蓄積したものであり、その過程において個人を特定する事がないように配慮した。

## C. 研究結果

対象患者の背景

在胎期間は予防投与無し群が 25 週 4 日（23 週 2 日～26 週 4 日）、予防投与有り群が 25 週 4 日（23 週 0 日～26 週 5 日）であった。出生体重は予防投与無し群が 750 g（476～990g）、予防投与有り群が 642 g（514～936g）であった。児の性別とアプガースコア、母体への陣痛抑制剤やステロイド投与、母体における前期破水の有無、母体への抗生剤使用、分娩法等について、両群間に差は認めなかった。胎盤病理組織による診断が行えた予防投与無し群 17 例と予防投与有り群 12 例中、絨毛膜羊膜炎の合併は予防投与無し群 6 例（35%）と予防投与有り群 8 例（67%）で、母体膣培養が行われた予防投与無し群 11 例と予防投与有り群 9 例中、真菌検出例は予防投与無し群 2 例（18%）と予防投与有り群 1 例（11%）で有意差は認めなかった。

急性期管理方法の比較

人工換気療法、経末梢的中心静脈カテーテルの使用等に有意差は認めなかったが、出生後のステロイド使用と臍動静脈カテーテルの留置が前期でより多く施行され、予防投与有り群で高濃度の保育器内加湿がより長期間なされていた。

真菌感染合併率と真菌検出率

真菌感染症合併例は予防投与無し群 7 例（37%）で死亡例が 4 例みられたのに対し、予防投与有り群は 1 例も認めず、有意に減少していた。予防投与無し群の死亡例の半数に真菌感染が関与しており、真菌感染を認めなかった予防投与有り群では生命的予後が改善していた。予防投与有り群は真菌検出例が 1 例も認めなかったのに対し、予防投与無し群の真菌検出例は 10 例(53%)で、検出された真菌はすべてカンジダ属であり、そのほとんどが *Candida albicans* で、他には *Candida glabrata* も認められた。真菌以外の感染症の合併について両期間に差は認めなかった。

合併症

消化管病変が予防投与無し群の 8 名(42%)から予防投与有り群の 1 例(8%)に有意に減少していた。治療を要した症候性動脈管開存症は予防投与無し群の 3 例(16%)から予防投与有り群の 8 例(62%)に有意に増加していた。その他の主要な合併症について差は認めなかった。

FLCZ の副作用

臨床症状に明らかに異常をきたした症例はなく、生後 1 ヶ月未満における白血球数の増加（予防投与無し群 13 例、予防投与有り群 6 例)、白血球数減少（予防投与無し群 5 例、予防投与有り群 0 例)、肝機能障害（予防投与無し群 1 例、予防投与有り群 1 例）などの検査値異常においても、有意差は認めなかった。

**D. 考察**

今回の検討から、在胎 27 週未満の超早産児に対する FLCZ の予防投与は真菌感染および検出例を有効に減少させ、これらの児の死亡率を劇的に改善させる結果に寄与することが示された。

真菌感染が減少した最大の理由が FLCZ 予防投与と判断した理由は、真菌以外の感染症の発症率には差が認めなかったためである（予防投与無し群 37%、予防投与有り群 31%)。出生後ステロイド投与も臍帯動静脈カテーテルの使用も真菌感染だけに特異的に関連しているわけではなく、感染症全般に影響するはずである。また、今回の検討対象から除外しているが、予防投与を行っていた期間中に FLCZ 予防投与を施行しなかった在胎 26 週で出生した 3 例中、1 例に真菌感染を発症した。この症例にはステロイドも臍帯動静脈カテーテルも共に使用していなかった。FLCZ 予防投与を施行しなかった症例のみに真菌感染合併例を認めたことは、治療時期による相違ではなく FLCZ 予防投与の直接的効果を強く示唆すると思われる。

今回の検討では、2～3 週間以内で終了する方法であったが、十分に真菌感染抑制効果が得られた。保育器内加湿が不要となり、経腸栄養が確立し、腸内細菌叢が安定し、カテーテル類の使用が減少する以降は、真菌感染の危険性が低いことが推測され、その後の FLCZ 予防投与は不要であると思われる。低出生体重児における FLCZ の薬物動態については研究されているが、3mg/kg/day を 2 日おきに投与する方法については治療量に比べ投与量が比べ少なく、今回の検討においても白血球数異常や肝機能障害などの FLCZ 投与による副作用は認めなかった。今回使用した投与量では、超早産児においても FLCZ 予防投与は安全であると考えられた。

**E. 結論**

超早産児に対する FLCZ の予防投与が真菌感染合併を有効に減少させ、その予後を改善させた。真菌感染症の頻度が高い施設では超早産児の予後を改善させる安全で、かつ有効な対策となりうると考えられた。

**F. 健康危機状況　なし**

**G. 研究発表**

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学会発表

なし

H. 知的財産権の出願・登録状況

1．特許取得　なし

2．実用新案登録　なし

3．その他　な

# Ⅲ．　研究成果の刊行に関する一覧表

# 研究成果の刊行に関する一覧表

| 著者氏名 | 論文タイトル | 発表誌 | 巻号 | ページ | 出版年 |
|---|---|---|---|---|---|
| Suka M, Yoshida K, Takezawa J | Impact of intensive care unit-acquired infection on hospital mortality in Japan: A multicenter cohort study | Environ Health Prev Med | 19 | 53-7 | 2004 |
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| Suka M, Yoshida K, Takezawa J | Association between APACHE II score and nosocomial infection in intensive care unit patients: A multicenter cohort study | Environ Health Prev Med | 9 | 262-5 | 2004 |
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| Wachino J, Doi Y, Yamane K, Shibata N, Yagi T, Kubota T, Ito H, Arakawa Y | Nosocomial spread of ceftazitime-resistant *Kledbsiella pneumoniae* strains producing a novel class A β-lactamase, ES-3, in a neonatal intensive care unit in Japan | Antimiocro Agent Chemother | 45 | 1960-67 | 2004 |

# Ⅳ．　研究成果の刊行物

# Impact of Intensive Care Unit-Acquired Infection on Hospital Mortality in Japan: A Multicenter Cohort Study

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*Original Article*

# Impact of Intensive Care Unit-Acquired Infection on Hospital Mortality in Japan: A Multicenter Cohort Study

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## Abstract:

**Objectives: To elucidate factors associated with hospital mortality in intensive care unit (ICU) patients and to evaluate the impact of ICU-acquired infection on hospital mortality in the context of the drug resistance of pathogens.**

**Methods: By using the Japanese Nosocomial Infection Surveillance (JANIS) database, 7,374 patients who were admitted to the 34 participating ICUs between July 2000 and May 2002, were aged 16 years or older, and who stayed in the ICU for 48 to 1,000 hours, did not transfer to another ICU, and did not become infected within 2 days after ICU admission, were followed up until hospital discharge or to Day 180 after ICU discharge. Adjusted hazard ratios (HRs) with the 95% confidence intervals (CIs) for hospital mortality were calculated using Cox's proportional hazard model.**

**Results: After adjusting for sex, age, and severity-of-illness (APACHE II score), a significantly higher HR for hospital mortality was found in ventilator use, central venous catheter use, and ICU-acquired drug-resistant infection, with a significantly lower HR in elective or urgent operations and urinary catheter use. The impact of ICU-acquired infection on hospital mortality was different between drug-susceptible pathogens (HR 1.11, 95% CI: 0.94-1.31) and drug-resistant pathogens (HR 1.42, 95% CI: 1.15-1.77).**

**Conclusions: The use of a ventilator or a central venous catheter, and ICU-acquired drug-resistant infection were associated with a high risk of hospital mortality in ICU patients. The potential impact on hospital mortality emphasizes the importance of preventive measures against ICU-acquired infections, especially those caused by drug-resistant pathogens.**

**Key words:** multicenter cohort study, hospital mortality, ICU, nosocomial infection, drug resistance

## Introduction

The intensive care unit (ICU) is known to be a hot spot of infections (1,2). The 1-day point-prevalence study of 1,417 ICUs in 17 Western European countries, so called the EPIC study, showed that the prevalence rate of infection in ICUs was 44.8%, and almost half of the infections were acquired in the ICU (20.6%) (3).

ICU-acquired infection is recognized as one of the most important determinants for the outcome of ICU patients. However, the precise relationship in terms of cause and effect between ICU-acquired infection and hospital mortality has yet to be defined. There have been few cohort studies in which ICU patients were followed up until hospital discharge. A cohort study of 28 ICUs in 8 countries showed that the hospital mortality rate in patients with ICU-acquired infection was 32.1%, against 12.1% of that in non-infected patients (4). These rates were crude and not adjusted for potential confounding factors (e.g., age, underlying disease, and severity-of-illness) (5,6). Moreover, the impact of ICU-acquired infection on hospital mortality might be affected by the drug resistance of pathogens (7).

In July 2000, Japanese Ministry of Health, Labour, and Welfare started the Japanese Nosocomial Infection Surveillance (JANIS) System, which consists of three components of ICU, laboratory, and hospitalwide surveillance (8,9,10). In the ICU component, all of the patients admitted to the participating ICUs are followed up until hospital discharge. By using the large cohort database of the JANIS System, we elucidated

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**Table 1 Age and sex distribution of the study population**

| | | All | Age, y.o. | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 16–24 | 25–34 | 35–44 | 45–54 | 55–64 | 65–74 | 75–84 | 85– |
| All | Alive | 6070 | 190 | 246 | 347 | 826 | 1339 | 1922 | 1035 | 165 |
| | Dead | 1304 | 31 | 54 | 54 | 164 | 232 | 376 | 292 | 101 |
| | % of dead | 17.7% | 14.0% | 18.0% | 13.5% | 16.6% | 14.8% | 16.4% | 22.0% | 38.0% |
| Men | Alive | 3934 | 98 | 145 | 218 | 583 | 929 | 1279 | 608 | 74 |
| | Dead | 828 | 16 | 29 | 38 | 118 | 150 | 246 | 173 | 58 |
| | % of dead | 17.4% | 14.0% | 16.7% | 14.8% | 16.8% | 13.9% | 16.1% | 22.2% | 43.9% |
| Women | Alive | 2136 | 92 | 101 | 129 | 243 | 410 | 643 | 427 | 91 |
| | Dead | 476 | 15 | 25 | 16 | 46 | 82 | 130 | 119 | 43 |
| | % of dead | 18.2% | 14.0% | 19.8% | 11.0% | 15.9% | 16.7% | 16.8% | 21.8% | 32.1% |

factors associated with hospital mortality in ICU patients and evaluated the impact of ICU-acquired infection on hospital mortality in the context of the drug resistance of pathogens.

## Subjects and Methods

A large cohort database was accumulated from the JANIS System (11). Details of data collection and definitions in the JANIS System have been described elsewhere (8,11,12). For all of the patients admitted to the 34 participating ICUs (mostly in national university hospitals) between July 2000 and May 2002, the following patient data were collected using a specific database-oriented software in the standardized forms: sex, age, underlying disease, severity-of-illness (APACHE II score (13)), ICU admission and discharge (date, time, and route), operation (elective and urgent), device use (ventilator, urinary catheter, and central venous catheter), infection (pneumonia, urinary tract infection, catheter-related bloodstream infection, sepsis, wound infection, and others), and hospital discharge (date and outcome). All types of infection were diagnosed according to the JANIS criteria (14). ICU-acquired infection was defined as a newly developed infection at least 2 days after ICU admission (15).

The cohort consisted of 7,374 eligible patients, aged 16 years or older, who stayed in ICU for 48 to 1,000 hours, did not transferred to another ICU, and did not become infected within 2 days after ICU admission. They were followed up until hospital discharge or to Day 180 after ICU discharge. Table 1 shows the age and sex distribution of the 7,374 ICU patients.

We paid special attention to the protection of anonymity and the confidentiality of the available data.

## Statistical analyses

The statistical analyses were performed with the Statistical Analysis Systems (SAS, version 8.2). Distributions of operation, device use, and ICU-acquired infections were compared by chi-square tests. Adjusted hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) were calculated using Cox's proportional hazard model (16).

## Results

Table 2 shows the relationship between operation or device use and hospital mortality. Compared with those who had no operation, those who had elective or urgent operations showed significantly lower rates of hospital mortality. The use of a ventilator or a central venous catheter was significantly associated with hospital mortality, while that of a urinary catheter was not.

**Table 2 Relationship between operation or device use and hospital mortality**

| | Alive | Dead | % of dead | |
|---|---|---|---|---|
| [Operation] | | | | |
| None | 2175 | 756 | 25.8% | |
| Elective | 2542 | 181 | 6.6% | |
| Urgent | 1353 | 367 | 21.3% | p<0.001 |
| [Ventilator] | | | | |
| Non-user | 2067 | 210 | 9.2% | |
| User | 4003 | 1094 | 21.5% | p<0.001 |
| [Urinary catheter] | | | | |
| Non-user | 275 | 75 | 21.4% | |
| User | 5795 | 1229 | 17.5% | p=0.06 |
| [Central venous catheter] | | | | |
| Non-user | 1457 | 198 | 12.0% | |
| User | 4613 | 1106 | 19.3% | p<0.001 |

Distributions were compared by chi-square tests.

Table 3 shows the relationship between ICU-acquired infection and hospital mortality. Overall, 678 patients (9.2%) had at least one episode of ICU-acquired infection. Drug-resistant pathogens were detected in 201 patients. The most common ICU-acquired infections were pneumonia (517 cases, 64%), followed by sepsis (106 cases, 13%), wound infection (102 cases, 13%), urinary tract infection (43 cases, 5%), and catheter-related bloodstream infection (42 cases, 5%). All types of ICU-acquired infection were significantly associated with hospital mortality. Compared with those who had no infection, those who had ICU-acquired infections caused by drug-susceptible and -resistant pathogens showed higher rates of hospital mortality. The rate of ICU-acquired infection caused by drug-resistant pathogens was higher than that by drug-susceptible pathogens, except for urinary tract infection, in which few cases of drug-resistant pathogens were observed.

Table 4 shows the HRs and the corresponding 95% CIs for hospital mortality. After adjusting for sex, age, and APACHE II score, a significantly higher HR for hospital mortality was found in ventilator use, central venous catheter use, and ICU-

**Table 3 Relationship between ICU-acquired infection and hospital mortality**

| | Alive | Dead | % of dead | |
|---|---|---|---|---|
| [All] | | | | |
| None | 5656 | 1040 | 15.5% | |
| Drug-susceptible | 305 | 172 | 36.1% | |
| Drug-resistant | 109 | 92 | 45.8% | p<0.01 |
| [Pneumonia] | | | | |
| None | 5756 | 1101 | 16.1% | |
| Drug-susceptible | 230 | 140 | 37.8% | |
| Drug-resistant | 84 | 63 | 42.9% | p<0.001 |
| [Urinary tract infection] | | | | |
| None | 6042 | 1289 | 17.6% | |
| Drug-susceptible | 25 | 15 | 37.5% | |
| Drug-resistant | 3 | 0 | 0.0% | p<0.01 |
| [Catheter-related bloodstream infection] | | | | |
| None | 6049 | 1277 | 17.4% | |
| Drug-susceptible | 18 | 18 | 50.0% | |
| Drug-resistant | 3 | 3 | 50.0% | p<0.001 |
| [Sepsis] | | | | |
| None | 6038 | 1230 | 16.9% | |
| Drug-susceptible | 24 | 52 | 68.4% | |
| Drug-resistant | 8 | 22 | 73.3% | p<0.001 |
| [Wound infection] | | | | |
| None | 6009 | 1263 | 17.4% | |
| Drug-susceptible | 44 | 28 | 38.9% | |
| Drug-resistant | 17 | 13 | 43.3% | p<0.001 |

Distributions were compared by chi-square tests.

**Table 4 Hazard ratios and the corresponding 95% confidence intervals for hospital mortality**

| | HR | 95% CI (lower–upper) |
|---|---|---|
| Sex (Women vs. Men) | 1.06 | (0.95–1.19) |
| Age, y.o. † | | |
| 45–54 | 1.19 | (0.94–1.49) |
| 55–64 | 1.06 | (0.85–1.31) |
| 65–74 | 1.11 | (0.91–1.35) |
| 75– | 1.33 | (1.09–1.62) |
| APACHE II score ‡ | | |
| 11–15 | 1.68 | (1.37–2.06) |
| 16–20 | 2.66 | (2.18–3.25) |
| 21–25 | 4.28 | (3.48–5.27) |
| 26–30 | 5.92 | (4.76–7.37) |
| 31– | 7.88 | (6.23–9.97) |
| Operation | | |
| Elective | 0.29 | (0.24–0.34) |
| Urgent | 0.68 | (0.59–0.77) |
| Ventilator | 1.78 | (1.49–2.12) |
| Urinary catheter | 0.70 | (0.54–0.90) |
| Central venous catheter | 1.23 | (1.04–1.47) |
| ICU-acquired infection | | |
| Drug-susceptible | 1.11 | (0.94–1.31) |
| Drug-resistant | 1.42 | (1.15–1.77) |

HR=hazard ratio, CI=confidence interval.
† compared with –44 y.o.
‡ compared with 0–10.

acquired infection caused by drug-resistant pathogens, with a significantly lower HR in elective or urgent operations and urinary catheter use. The impact of ICU-acquired infection on hospital mortality was different between drug-susceptible pathogens (HR 1.11, 95% CI: 0.94-1.31) and drug-resistant pathogens (HR 1.42, 95% CI: 1.15-1.77).

## Discussion

By using the large cohort database of the JANIS System, we elucidated factors associated with hospital mortality in ICU patients and evaluated the impact of ICU-acquired infection on hospital mortality in the context of the drug resistance of pathogens. To our knowledge, this is the fist multicenter cohort study on hospital mortality in ICU patients in Japan. The JANIS System attempts to provide a uniform approach of data collection and definitions to participating ICUs. Data are collected using a specific database-oriented software in the standardized forms. All types of infection are diagnosed according to the JANIS criteria. Thanks to the JANIS database, we may further obtain reliable findings from standardized data.

The crude hospital mortality rate in the patients with ICU-acquired infection caused by drug-susceptible and -resistant pathogens was 36.1% and 45.8%, respectively, against 15.5% of that in the non-infected patients (Table 3). These rates are somewhat higher than those shown in another cohort study of 28 ICUs in 8 countries (32.1% in patients with ICU-acquired infection and 12.1% in non-infected patients)(4). Because of the difference in ICU type (surgical unit dominant vs. medical unit dominant), minimal length of ICU stay (48 hours vs. 24 hours), and other settings between the two studies, it is difficult to compare the rates in detail. Multivariate analysis, adjusting for sex, age, and APACHE II score, showed that the risk of hospital mortality in the patients with ICU-acquired infection caused by drug-resistant pathogens was 1.4 times higher than that in the non-infected patients (Table 4). This result supports the importance of preventive measures against ICU-acquired infections, especially those caused by drug-resistant pathogens.

The EPIC study showed that the impact of ICU-acquired infection on ICU mortality might vary according to type of infection; the highest odds ratio was found in sepsis (3.50), followed by pneumonia (1.91) and bloodstream infection (1.73) (3). Moreover, several studies showed that inadequate administration of autibiotics might be an important determinant of hospital mortality (17,18). When we evaluated the impact of ICU-acquired infection on hospital mortality in the context of types of infection, only sepsis was significantly associated with a high risk of hospital mortality (HR 2.14, 95% CI:1.62-2.84) (data not shown). The impact of ICU-acquired infection on hospital mortality, as well as that on ICU mortality, might vary according to type of infection. In the future, the increase in the risk of hospital mortality in patients with ICU-acquired infection will be evaluated in detail, taking into account type of infection and antibiotics use in addition to the drug resistance of pathogens.

In the multivariate analysis, the risk of hospital mortality was increased in those aged 75 years or older and also increased

with APACHE II score. These results support the importance of adjustment for age and severity-of-illness as major confounding factors.

The risk of hospital mortality in those who had elective or urgent operations was lower than that in those who had no operation. Those who had operations were likely to have a better physical strength before ICU administration. Moreover, some other factors (e.g., underlying disease, preoperative antibiotics use, and length of ICU stay) (19) might contribute to the low risk of hospital mortality in those who had operations.

Each device use was significantly associated with hospital mortality. The risks of hospital mortality in users of ventilators and central venous catheters were 1.8 and 1.2 times higher than that in non-users. Because we could not take into account duration of device use, the impact of device use on hospital mortality might be underestimated or overestimated. Those who use a device are likely to be in a severe condition. Moreover, the longer a device is used, the more likely it is to cause infections (20). In this study, the utilization rates of ventilator and central venous catheter were increased with APACHE II score (Table 5). Also, ICU-acquired infections were more frequently observed in users of ventilator and central venous catheter (Table 6). Because both APACHE II score and ICU-acquired infection were simultaneously incorporated into Cox's proportional hazard model, their confounding effects might be minimized. However, the impact of ICU-acquired infection on hospital mortality might be underestimated or overestimated. Further studies, such as path analysis, may help in the understanding of the details of the relationships in terms of cause and effect among device use, APACHE II score, ICU-acquired infection, and hospital mortality. Contrary to our expectation, the risk of hospital mortality in users of urinary catheter was lower than that in non-users. It might be an apparent relationship caused by the high utilization rate of urinary catheter (95%). It is difficult to explain the low risk in users of urinary catheter and to find a conclusive answer on the relationship between urinary catheter use and hospital mortality based on the finding of this study. When we performed the multivariate analysis again, excluding urinary catheter use from Cox's proportional hazard model, there was no marked difference in the impact of ICU-acquired infection on hospital mortality (data not shown).

This study may provide valuable information on hospital mortality in ICU patients in Japan. However, most of the participating ICUs are in national university hospitals, where the levels of hospital infection control are likely to be higher in Japan. The findings of this study may not represent the average for Japanese hospitals. Further studies may be required to confirm our findings in other hospitals.

In addition to the factors examined in this study, a number of factors have been found to be associated with hospital and ICU mortality. Underlying diseases (e.g., renal failure, acute respiratory failure, coma, neurologic disease) and medical treatments (e.g., steroids or chemotherapy) have been associated with increased hospital mortality (19,21). As mentioned above, inadequate treatment of infections might be an important determinant of hospital mortality (17,18). Medical ICU patients have a higher hospital mortality rate than surgical ICU patients (19). Some ICU organizational characteristics have been found to be associated with hospital mortality (22). A systematic review showed that high-intensity ICU physician staffing (i.e., the intensivist is the patient's primary attending physician, or, the intensivist is not the patient's primary physician, but every patient receives a critical care consultation) was associated with reduced hospital mortality (23). Currently, we are proceeding with a review of the JANIS System and an upgrade of its

**Table 5 Relationship between device use and APACHE II score**

| | APACHE II score | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0–10 | 11–15 | 16–20 | 21–25 | 26–30 | 31– | |
| [Ventilator] | | | | | | | |
| Non-user | 1322 | 548 | 238 | 107 | 42 | 20 | |
| User | 1677 | 1261 | 973 | 601 | 366 | 219 | |
| % of user | 55.9% | 69.7% | 80.3% | 84.9% | 89.7% | 91.6% | p<0.001 |
| [Urinary catheter] | | | | | | | |
| Non-user | 130 | 62 | 64 | 42 | 29 | 23 | |
| User | 2869 | 1747 | 1147 | 666 | 379 | 216 | |
| % of user | 95.7% | 96.6% | 94.7% | 94.1% | 92.9% | 90.4% | p<0.001 |
| [Central venous catheter] | | | | | | | |
| Non-user | 865 | 354 | 230 | 124 | 60 | 22 | |
| User | 2134 | 1455 | 981 | 584 | 348 | 217 | |
| % of user | 71.2% | 80.4% | 81.0% | 82.5% | 85.3% | 90.8% | p<0.001 |

Distributions were compared by chi-square tests.

**Table 6 Relationship between device use and ICU-acquired infection**

| | ICU-acquired infection | | | % of infection | |
|---|---|---|---|---|---|
| | None | Drug-susceptible | Drug-resistant | | |
| [Ventilator] | | | | | |
| Non-user | 1296 | 59 | 22 | 5.9% | |
| User | 4500 | 418 | 179 | 11.7% | p<0.001 |
| [Urinary catheter] | | | | | |
| Non-user | 323 | 18 | 9 | 7.7% | |
| User | 6373 | 459 | 192 | 9.3% | p=0.6 |
| [Central venous catheter] | | | | | |
| Non-user | 1581 | 59 | 15 | 4.5% | |
| User | 5115 | 418 | 186 | 10.6% | p<0.001 |

Distributions were compared by chi-square tests.

database. We will be able to study further details of the risk of hospital mortality in ICU patients.

In conclusion, the use of a ventilator or a central venous catheter, and ICU-acquired drug-resistant infection are associated with a high risk of hospital mortality in ICU patients. The potential impact on hospital mortality emphasizes the importance of preventive measures against ICU-acquired infections, especially those caused by drug-resistant pathogens. Because drug resistance is largely due to inadequate administration of antibiotics, clinicians should consider drug resistance as part of their routine treatment plans (1,2,20). Quality control of antibiotics use by providing locally adapted guidelines for prudent antibiotics use is recommended (2). As a matter of course, basic infection control practices are indispensable to combat the spread of drug-resistant infections (1,20,24). Surveillance systems contribute to detecting drug-resistant infections, feedback on infection control performance, and promoting research to prevent drug-resistant infections. Paying careful attention to this problem at the local ICU level, using a multidisciplinary approach, will have the greatest likelihood of limiting the development and spread of drug-resistant infections (24).

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superficial layers of skin, are responsible for most health care related infections and the spread of antimicrobial resistance. This group includes organisms such as *Staphylococcus aureus*, Gram-negative bacilli and *Candida* species amongst them.

There are 2 different methods for hand hygiene. In the traditional method, hands should be washed thoroughly with soap and water for at least one minute, and a disposable towel should be used to dry hands and perhaps to close the faucet. With mechanical friction, microorganisms are removed from the skin and hair follicles. It is now thought that such careful hand washing is essential only when hands are soiled with body fluids. In general, it takes approximately 2 minutes to complete such a hand-washing task. It is estimated that if good hand washing is performed for 3 episodes per hour, nurses may have to spend about one fifth of their time washing hands during an 8-hour shift.

The emerging alternative is alcohol-based hand rubbing solutions and gels. The use of alcohol-based hand rubs is being recommended in most other circumstances in which hand hygiene is required. Alcohol has bactericidal properties that most hand washing soaps do not have. A much shorter time is needed to achieve a significant reduction in bacterial colony counts when using alcohol based hand rubs. These products also have some important virucidal activity. Also, alcohol-based hand rubs can be used while traveling between the points of contact with the patient to other areas of work, or even while traveling to the next patient.

The use of powder-free gloves reduces the need for hand washing; however, it does not obviate the need for hand hygiene. Alcohol-based hand rubs should be used after removing gloves. Needless to say, a new pair of gloves should be used for each patient contact. Trampuz et al suggest that alcohol-based hand rubs are also easier on hands than repeated washing with soap and water. Alcohol rubs should be stored away from high temperatures. At present, it is thought that the emergence of microbial resistance is less likely against alcohol-based formulations. It is important to remember that alcohol based hand rubs are to be used only when direct contamination of hands with body fluids has not occurred. The risk of wearing rings and artificial fingernails, which may act as harbingers of bacterial contamination, is highlighted in the article. Based on the available scientific evidence, Trampuz et al suggest that alcohol-based hand rubs should be used liberally and regularly to reduce nosocomial infections.

■ **COMMENT BY UDAY B. NANAVATY, MD**

Good hand hygiene by health care personnel is vital to reduce nosocomial infection rates. Maintaining good hand hygiene is a moral duty as well. Unfortunately, routine compliance rates with good hand hygiene are ridiculously low. Most studies suggest that hand hygiene compliance rates in hospital settings are between 20 to 40%. Hospital and system wide projects including education and surveillance by camera and other electronic devices improve compliance rates. Unfortunately, even with these expensive interventions, compliance rates approach only about 70% at best. Imagine if restaurant workers had hand hygiene rates of 40% or less! The country would be reeling with gastrointestinal morbidity and the food industry would be out of business. Before the bugs on our hands get us out of our business, it is important that we get rid of them, as best and as frequently as possible. ■

*Special Feature*

# Hospital Mortality and ICU-Acquired Infection

*By Jun Takezawa, MD*

### Risk Factors for the ICU-Acquired Infection

SEVERAL FACTORS ARE CONSIDERED TO BE ASSOCIATED with the development of nosocomial infections in the ICU (*see Table 1*). Among them, indwelling devices that directly contact the blood and mucosal membrane such as the central venous catheter, urinary tract catheter and endotracheal tube are considered to be the most responsible risk factors in the development of nosocomial infections. These devices are placed into the patient and manipulated by the medical practitioner, and referred to as external risk factors. These device-related external risk factors are associated with the length of

**Table 1**
**Risk Factors for the Development of ICU-Acquired Infection**

| Risk | |
|---|---|
| Internal risk | Age, Gender, Original disease, Severity of illness, Comorbidity |
| External risk | • Device: Central venous catheter, Ventilator, Urinary tract catheter<br>• Drugs: Antibiotics, immunosuppressives<br>• Intervention/Operation Infection Control: hygienic procedure, Manual, Surveillance, Education<br>• Therapeutic and nursing capability Monitoring Organizational characteristics: Open/Closed, Staffing |

time the device remains in the patient. However, they are also associated with the frequency of manipulations of the device, such as bolus injection and exchanges of the infusion bottles and lines, especially for indwelling central venous catheters. In addition to the length and/or frequency of exposure to the risk device, the hygienic management, behavior pattern of antibiotic administration, level of infection control, and patient management (therapeutic, nursing, monitoring, staffing, and organizational) also play a role, along with the external risk factors, in the development of nosocomial infections. On the other hand, the risk factor inherent to the patient is referred as an internal risk factor. Such internal risk factors include age, gender, severity of illness, immunological competence, comorbidity, and so on.

In order to accomplish an inter-institutional comparison on infection rate, both internal and external risk factors should be adjusted. Among the risk factors indicated above, the internal risk may be adjusted by using measures of illness severity such as the APACHE score, but the external risk can only be adjusted by device utilization days. Therefore, the difference in infection rates adjusted by the above two risk factors is attributable to the other remaining external risk factors, most of which are related to both the patient and ICU management.

### Purpose of Surveillance

The purpose of the surveillance is 1) to identify the outbreak of nosocomial infections (although outbreaks are usually readily noticed by ICU practitioners); 2) to provide data on infection control to be pursued by ICU practitioners in quality improvement; 3) to obtain the incidence and prevalence of nosocomial infections from the viewpoint of public health; and 4) to provide for inter-institutional comparisons with respect to preventive programs and practice in managing nosocomial infections by the respective institutions.

When surveillance is conducted for the purpose of inter-institutional comparison of the nosocomial infection rate, all risk factors for ICU-acquired infections should be adjusted. The National Nosocomial Infection Surveillance (NNIS) system, which is run by the US Centers for Disease Control and Prevention (CDC), apparently uses only external risk-adjusted infection rates for inter-institutional comparison. The severity of illness in NNIS employs the device utilization ratio, which is calculated as the length of days the devices are in use divided by the number of patient days. Use of this ratio is based on the assumption that the severely ill patient requires long-term use of the devices for efficient and safer management. However, the device utilization ratio, as well as APACHE and SAPS scoring systems, which are frequently used for stratifying severity of illness in terms of mortality, are not proved to be related to the acquisition of nosocomial infections in the ICU, in part because the most severely ill patients die quickly. Therefore, patients who die within 24 hours after admission to the ICU are excluded for inter-hospital comparison of the performance of ICUs.

In the NNIS system, risk-adjusted infection rate is compared within the individual types of ICUs, such as neuro-ICU, coronary-CU, and surgical-ICU, which implies that the original disease is taken into account as an internal risk factor. However, because all the internal risk factors are not included in the NNIS system, the exact effect of ICU-acquired infections on

**Table 2**

**The Effect of ICU-Acquired Infections on Hospital Mortality**

| | # of pts | drug-susceptible | drug-resistant | *P*-value |
|---|---|---|---|---|
| Ventilator associated pneumonia | | | | |
| Alive | 5756 | 230 | 84 | — |
| Dead | 1101 | 140 | 63 | — |
| % of dead | 16.1 | 37.8 | 42.9 | < 0.001 |
| Urinary tract infection | | | | |
| Alive | 6042 | 25 | 3 | — |
| Dead | 1289 | 15 | 0 | — |
| % of dead | 17.6 | 37.5 | 0 | < 0.01 |
| Catheter-related bloodstream infections | | | | |
| Alive | 6049 | 18 | 3 | — |
| Dead | 1277 | 18 | 3 | — |
| % of dead | 17.4 | 50.0 | 50.0 | < 0.001 |
| Sepsis | | | | |
| Alive | 6038 | 24 | 8 | — |
| Dead | 1230 | 52 | 22 | — |
| % of dead | 16.9 | 68.4 | 73.3 | < 0.001 |
| Surgical site infection | | | | |
| Alive | 6009 | 44 | 17 | — |
| Dead | 1263 | 28 | 13 | — |
| % of dead | 17.4 | 38.9 | 43.3 | < 0.001 |

The total numbers of the patients are different among the ICU-acquired infections because of a lack of available data.

*Adapted from: Suka M, et al. Environ Health Prev Med. (in press).*

hospital mortality is unknown.

### ICU-Acquired Infection and Hospital Mortality

Although the incidence of ICU-acquired infection is recognized as an important determinant of outcome for ICU patients, the precise relationship between ICU-acquired infection and hospital mortality has yet to be defined. A 1-day point-prevalence study for 1417 ICUs from 17 western European countries, called the EPIC study, showed that a prevalence rate of infection in ICUs was 44.8%, and almost half of the infections were acquired in the ICU (20.6%).[1] The EPIC study showed that the impact of ICU-acquired infection on ICU mortality might vary according to the types of infection; the highest odds ratio was found in sepsis (3.50), followed by pneumonia (1.91) and blood stream infection (1.73). Moreover, several studies showed that inadequate treatment of infections might be an important determinant of hospital mortality.[2,3]

There have been few cohort studies in which the patients discharged from the ICU were followed up until hospital discharge. One cohort study involving 28 ICUs from 8 countries showed that the hospital mortality rate in patients with ICU-acquired infection was 32.1%, compared with 12.1% in patients without ICU-acquired infections.[4] These rates were crude and not adjusted for potential confounders (eg, age, underlying disease, and severity of illness).[5,6] Moreover, the impact of ICU-acquired infection on hospital mortality might be affected by drug-resistant pathogens.[7]

**Table 3**
**Factors Associated with Hospital Mortality[8]**

| | HR | 95% CI (lower-upper) |
|---|---|---|
| Sex (vs Man) | 1.06 | (0.95-1.19) |
| **Age (years)*** | | |
| 45-54 | 1.19 | (0.94-1.49) |
| 55-64 | 1.06 | (0.85-1.31) |
| 65-74 | 1.11 | (0.91-1.35) |
| 75- | 1.33 | (1.09-1.62) |
| **APACHE II score**** | | |
| 11-15 | 1.68 | (1.37-2.06) |
| 16-20 | 2.66 | (2.18-3.25) |
| 21-25 | 4.28 | (3.48-5.27) |
| 26-30 | 5.92 | (4.76-7.37) |
| 31- | 7.88 | (6.23-9.97) |
| **Operation** | | |
| Elective | 0.29 | (0.24-0.34) |
| Urgent | 0.68 | (0.59-0.77) |
| Ventilator | 1.78- | (1.49-2.12) |
| Urinary catheter | 0.70 | (0.54-0.90) |
| CV catheter | 1.23 | (1.04-1.47) |
| **ICU-acquired infection** | | |
| Drug-susceptible | 1.11 | (0.94-1.31) |
| Drug-resistant | 1.42 | (1.15-1.77) |

HR = hazard ratio, CI = confidence interval,
* = compared to 16-44 years, ** = compared to 0-10.

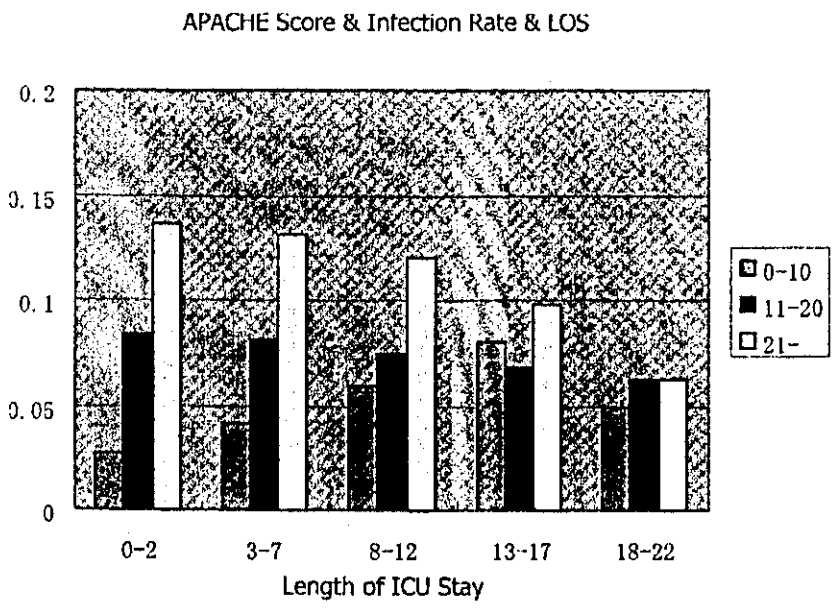
### JANIS Database Analysis

The Japanese Nosocomial Infection Surveillance (JANIS) system, started in 2000 by the Ministry of Health, Labor, and Welfare, collected data on 7374 patients admitted to the 34 participating ICUs between July 2000 and May 2002. The data used for their analysis is from patients discharged from ICU who were aged 16 years or older, whose ICU stay was from 48 to 1000 hours, who had not transferred to another ICU, and who had no infection diagnosed within 2 days after ICU admission. These patients were followed up until hospital discharge or the 180th day after ICU discharge. Adjusted hazard ratios (HRs) with their 95% confidence intervals (CIs) for hospital mortality were calculated using a Cox's proportional hazard model.[8]

Table 2 shows the effect of ICU-acquired infections on hospital mortality in the JANIS data. Overall, 678 patients (9.2%) had at least one ICU-acquired infection. Drug-resistant pathogens were detected in 201 patients. The most common ICU-acquired infections were ventilator-associated pneumonia (VAP, 517 cases, 64%), followed by sepsis (106 cases, 13%), surgical site infections (102 cases, 13%), urinary catheter-related infections (43 cases, 5%), and catheter-related blood stream infections (42 cases, 5%). All types of ICU-acquired infections were significantly associated with hospital mortality. Compared to patients who had no infection, those infected by drug-susceptible and drug-resistant pathogens had significantly higher rates of hospital mortality (shown as *P* value). The mortality rate with drug-resistant pathogens was higher than that with drug-susceptible pathogens, except for urinary tract infection in which few cases of drug-resistant pathogens were observed (not shown here).

Table 3 shows hazard ratios and their corresponding 95% confidence intervals for hospital mortality. After adjusting for sex, age, and APACHE II score, significantly higher HR for hospital mortality was found in respirator, central venous catheter, and ICU-acquired infection caused by drug-resistant pathogens, with significantly lower HR for elective and urgent operation and

**Figure**




*Adapted from: Suka M, et al. Environ Health Prev Med. (In Press).*

urinary catheter. The impact of ICU-acquired infection on hospital mortality was different between drug-sensitive pathogens (HR, 1.11; 95% CI, 0.94-1.31) and drug-resistant pathogens (HR, 1.42; 95% CI, 1.15-1.77).

### Severity of Illness and ICU-Acquired Infection

It is still unknown whether severity of illness is related to the development of ICU-acquired infections. When the incidence of ICU-acquired infections is evaluated in terms of severity of illness along with the ICU stay, the incidence of ICU-acquired infections along the ICU days is different among the severity of illness (*see Figure*).[8] In the most severely ill patients, the incidence of ICU-acquired infections is highest in the early phase of ICU admission, while in the least severely ill patients, the incidence of ICU-acquired infections is low in the early phase, but is increased along the ICU stay up to 20 days. In moderately ill patients, the incidence ICU-acquired infections do not change markedly along the ICU stay. Therefore, severity affects the incidence ICU-acquired infections; however, this effect on ICU-acquired infections is inversed depending on the severity of illness. In this sense, the general concept that the more severely ill the patients are, the more they develop nosocomial infections is not verified.

### Performance Measurement of ICUS

Performance of the ICU is usually measured in terms of outcome and process. The incidence of ICU-acquired infection is classified as the process evaluation, while hospital mortality is classified as outcome evaluation. However, the sensitivity of the outcome measurement by hospital mortality is low, because the relatively small numbers of the patients die during the hospital admission. Additionally, so many confounders are associated with the hospital mortality of ICU patients, which include original disease, severity of illness, development of complications (medical errors and nosocomial infections), patient management (therapeutic, nursing and monitoring capabilities), demographical characteristics (age and gender of the patients), and organizational characteristics (open or closed ICU, staffing). Because the magnitude of contribution of those confounders on mortality is not prioritized, it is extremely difficult to evaluate ICU performance on an individual confounder (risk factor) basis. It is of most importance to develop a new statistical model to measure both overall and individual confounder-based performance of the ICU. The ICU-acquired infection is one of the most important confounders (risk factors) for the measurement of ICU performance. It is concluded that performance of the ICU is improved by improving the individual risk factors; however, it is extremely difficult to achieve it by just monitoring the overall risk-adjusted hospital mortality of the patients discharged from the ICU. ■

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# CME / CE Questions

8. **Patients admitted to the ICU at night or on a weekend are more likely to die during that hospitalization because:**
   a. board-certified intensivists are less likely to be immediately available then;
   b. staffing of ICU nurses and respiratory therapists is less;
   c. important diagnostic tests and consultations are less immediately available;
   d. all of the above
   e. their severity of illness is greater

9. **Which of the following statements is true about hospital mortality in relation to when patients are admitted to the ICU?**
   a. Mortality is higher in patients admitted at night.
   b. Mortality is higher in patients admitted on weekends.
   c. Both of the above
   d. None of the above

10. **Based on a decision analysis model, the best strategy for managing late onset VAP in patients who had been mechanically ventilated for 7 days was:**
   a. mini-BAL and 2 antibiotic coverage.
   b. bronchoscopy and three antibiotic coverage.
   c. mini-BAL and three antibiotic coverage.
   d. 3 antibiotics, no diagnostic testing.
   e. antibiotics after results of diagnostic tests are available.

11. **As compared to culturing endotracheal aspirates or bronchoscopically obtained bronchoalveolar lavage (BAL) fluid, the non-bronchoscopic mini-BAL technique for diagnosing VAP:**
   a. decreased both costs and antibiotic use.
   b. decreased costs but increased antibiotic use.
   c. increased both costs and antibiotic use.
   d. increased costs but decreased antibiotic use.
   e. had no effect on either cost or antibiotic use.

12. **With the goal of reducing nosocomial infection rate in mind, good hand washing is required. All the following are true about hand washing *except*?**
   a. Good hand washing can be accomplished in 20 seconds with use of bactericidal soaps.
   b. Good hand washing should be followed by drying of hands with disposable towels.
   c. Good hand washing works mostly by the mechanical removal of organisms.
   d. Good hand washing would require at least one minute of hand washing.
   e. All of the above

13. **All the following are advantages of alcohol-based hand rubs *except* which statement?**
   a. They completely eliminate the need for hand washing.
   b. They reduce the time required for hand hygiene in certain situations.
   c. Alcohol-based hand rubs may be more gentle to the skin than soaps.
   d. Alcohol based hand rubs have bactericidal and virucidal properties.

14. **Which of the following are internal (as opposed to external) risk factors for ICU-acquired infection?**
   a. Monitoring
   b. Antibiotics administered
   c. Severity of illness
   d. All of the above
   e. None of the above

**Answers:** 8 (e); 9 (c); 10(c); 11 (a); 12 (a); 13 (a); 14 (c)

# CME / CE Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.



## In Future Issues:

**Hyperoxia Ineffective In Preventing Infection**