ORIGINAL ARTICLE

# Utilisation and outcome of renal replacement therapy in an Asian tertiary intensive care unit

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**Objectives** To determine the period prevalence, demographic characteristics, cost of treatment, and outcomes of patients admitted to the intensive care unit for continuous renal replacement therapy.

**Design** Descriptive case series.

**Setting** Intensive Care Unit in a Hong Kong tertiary referral, teaching hospital.

**Patients** All patients admitted to the Intensive Care Unit from January to December 2007 who underwent continuous renal replacement therapy.

**Main outcome measures** Period prevalence of continuous renal replacement therapy, patient demographic data, referral sources by specialty and hospital location, diagnosis, daily cost of disposable items, duration of renal replacement therapy, intensive care unit length of stay, and hospital mortality.

**Results** Of 1652 patients admitted to the intensive care unit over a 12-month period, 131 (8%) underwent continuous renal replacement therapy, of whom 56% were admitted from general wards (the department of medicine being the source of 59% of referrals). The median age of these continuous renal replacement therapy patients was 67 (interquartile range, 55-76) years, with a slight male predominance (66%). The mean APACHE II score of the patients was 29 (standard deviation, 7). Chronic renal failure requiring either haemodialysis or peritoneal dialysis was present in 20/131 (15%) patients. Sepsis was the diagnosis most commonly associated with renal failure deemed to warrant continuous renal replacement therapy (43%). The median duration of such continuous therapy was 55 (interquartile range, 25-93) hours and the median intensive care unit length of stay was 120 (interquartile range, 51-289) hours. The mean daily cost of disposables for the provision of continuous renal replacement therapy was HK$3510. The overall intensive care unit mortality of patients having continuous renal replacement therapy was 38% and the hospital mortality was 53%. The corresponding rates for patients with acute renal failure were 45% and 56%, respectively. Patients undergoing continuous renal replacement therapy had prolonged intensive care unit stays (120 vs 24 hours; $P<0.05$) and higher corresponding hospital mortality rates (53% vs 20%; $P<0.001$) compared to those not having such therapy.

**Conclusion** The 8% period prevalence of patients admitted to the intensive care unit undergoing continuous renal replacement therapy was somewhat higher than in recently published reports in the international literature. However intensive care unit and hospital mortality rates for such patients were lower than previously reported. The corresponding total daily cost of relevant disposables was similar to costs reported internationally, whilst the length of intensive care unit stays for our cohort were relatively short.

**Key words**
Acute kidney injury; Intensive care units; Mortality; Renal replacement therapy

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**New knowledge added by this study**

- The period prevalence of acute renal failure treated by continuous renal replacement therapy (CRRT) among intensive care unit (ICU) patients in Hong Kong is high.
- After adjustment for severity of illness, mortality among patients offered CRRT was higher than that in other ICU patients.

**Implications for clinical practice or policy**

- Patients undergoing CRRT in Hong Kong ICUs are resource intensive and can be expected to have a median ICU length of stay of 120 hours.
- Accurate calculation of CRRT dosage may avoid excessive use of replacement solutions and be an efficient way to contain cost.

## 一所亞洲三級醫院深切治療部的腎臟替代治療的使用及結果

**目的** 探討深切治療部內接受連續性腎臟替代治療的病人在治療期間的患病率、特徵、治療成本及結果。

**設計** 描述性病例系列。

**安排** 香港一所大學教學醫院的深切治療部。

**患者** 2007年入住深切治療部並接受連續性腎臟替代治療的病人。

**主要結果測量** 連續性腎臟替代治療期間的患病率、患者特徵、轉介病人的醫院及專科、診斷、每日所使用一次性用品的價格、治療期、深切治療部內留醫的日數和醫院死亡率。

**結果** 在12個月的研究期間，共1652名病人入住深切治療部，其中131名（8%）病人接受連續性腎臟替代治療，他們當中56%由普通病房轉介（內科漸其中的59%）。接受連續性腎臟替代治療的病人的年齡中位數為67歲（四分位距55至76歲）；男性居多（66%）。APACHE II平均分為29分（標準差7分）。131人中，無論是進行血液透析或腹膜透析的慢性腎功能衰竭患者有20人（15%）。腎衰竭並需要接受連續性腎臟替代治療病人當中最常見的是敗血症（43%）。接受連續性腎臟替代治療期的中位數為55小時（四分位距25至93小時），入住深切治療部的中位數為120小時（四分位距51至289小時）。每日使用一次性用品的平均價格為港幣$3510。總括而言，接受連續性腎臟替代治療的病人，其深切治療部和醫院死亡率分別為38%和53%。而患有急性腎衰竭的病人則分別為45%和56%。病人中需接受連續性腎臟替代治療的比未有接受此治療的有較長深切治療入住期（120小時比24小時；$P<0.05$），並有較高的醫院死亡率（53%比20%；$P<0.001$）。

**結論** 入住深切治療部而又接受連續性腎臟替代治療的病人的病發率為8%，雖然此數字略高於近年國際文獻發表的研究報告，但其深切治療部和醫院死亡率卻相對較低。每日使用一次性用品的平均價格與國際文獻發表的數據相近。本研究的病人入住深切治療部的日子相對較短。


## Introduction

Acute renal failure (ARF) is a common problem in the intensive care unit (ICU) and is associated with increased morbidity, higher costs, and greater mortality. As a result of the different definitions and inclusion criteria used, the period prevalence reported varies widely from 1 to 25% in single-centre studies, but up to 71% in multicentre studies. In a recent multinational study, the period prevalence of ARF in ICUs was noted to be about 6% and up to two-thirds underwent continuous renal replacement therapy (CRRT).[1] There is little Hong Kong data describing the prevalence, demographic characteristics, and outcome of such patients who develop ARF and undergoing CRRT. This information is important, as debate continues regarding the costs and benefits of CRRT.[2]

## Methods

This audit was conducted at the Prince of Wales Hospital ICU, a tertiary referral centre serving all specialties including neurosurgery and cardiac surgery. The unit has 20 general medical/surgical ICU beds and two cardiac surgical beds. Renal replacement therapy is prescribed and managed by specialist intensivists, and delivered by trained intensive care nursing staff.

We retrospectively audited all patients admitted to the ICU between January 2007 and December 2007 who underwent CRRT. Standardised renal replacement therapy prescription and audit forms for the audit period were collected. Data recorded were compared with the electronic adult patient database system (AORTIC, Australia and New Zealand Intensive Care Society) to ensure that all relevant patients were included in the audit. Clinical records of individual patients were reviewed to retrieve demographic and outcome data. Information was collected to determine demographic characteristics, referral patterns, severity of illness, duration of CRRT, ICU length of stay, ICU mortality, hospital mortality, and estimated daily costs of disposables for CRRT. In our institution, CRRT is primarily used to treat the sequelae of renal failure (uraemia, severe azotemia with fluid overload, electrolyte disturbances, or metabolic acidosis). Patients with chronic renal failure (CRF) were defined as those undergoing regular dialysis therapy prior to ICU admission. Data from patients with ARF undergoing CRRT, and those with CRF were analysed separately when appropriate. For clinical and logistic reasons, the use of intermittent haemodialysis (IHD) in the ICU was rare and patients who underwent IHD in the ICU were excluded from the study.

All CRRT was conducted with Gambro PRISMA renal replacement units, using AN-69 polyacrylonitrile predilution membrane dialysers. Vascular access was obtained using either MEDCOMP 11F (15 or 20 cm) or Gamcath 13F (15 or 20 cm) venovenous access catheters. When indicated, anticoagulation was routinely achieved with low-dose unfractionated heparin. The predominant CRRT modalities were continuous venovenous haemofiltration and continuous venovenous haemodiafiltration.

### Statistical analysis

Data management and statistical analysis were performed using the Statistical Package for the Social Sciences (Windows version 14.0; SPSS Inc, Chicago [IL], US). The Kolmogorov-Smirnov test was used to analyse for normality of distributions. Summary data are presented as medians with interquartile ranges (IQRs) for non-continuous data, and as means with 95% confidence intervals (CIs) for normally distributed continuous data. Continuous data with a sufficiently normal distribution were compared using Student's *t* test. The Mann-Whitney *U* test was used to analyse ordinal variables. Categorical data were analysed by the Chi squared test.

The APACHE (Acute Physiology and Chronic Health Evaluation) II scoring system was used to determine the severity of patient illness and mortality risk. The score is calculated from 12 physiological parameters measured during the first 24 hours after admission. Up to four points are assigned to each physiological variable according to its most abnormal value. Additional points are assigned for age, history of severe clinical conditions, and the type of surgical status. The total number of points gives a score ranging from 0 to 71; increasing scores represent a greater illness severity. Mortality risk is derived by combining the APACHE II score with the patient's diagnostic score.[3]

The risk-adjusted standardised mortality ratio ($SMR_{RA}$) is the ratio of actual mortality to predicted mortality risk derived from the APACHE II score. When the calculated $SMR_{RA}$ is less than one, it indicates that fewer such patients should die than expected, and vice versa for scores greater than one. The $SMR_{RA}$ with 95% CIs was calculated for patients receiving CRRT,

Table 1. Demographic data for all patients having continuous renal replacement therapy; those for acute renal failure patients are shown separately where appropriate

| Characteristics* | Data† |
|---|---|
| Age (years) | 67 (55-76) |
| Sex (female) | 44 (34%) |
| APACHE II score | |
| All patients | 29 ± 7 |
| Patients with ARF | 28 ± 7 |
| Type of renal failure | |
| ARF requiring dialysis | 111 (85%) |
| CRF requiring dialysis | 20 (15%) |
| Admission source | |
| Ward | 73 (56%) |
| Emergency department | 35 (27%) |
| Operating theatre | 18 (14%) |
| Other hospitals | 5 (3%) |
| Renal function markers prior to CRRT | |
| All patients | |
| Creatinine (μmol/L) | 287 (190-476) |
| Urea (mmol/L) | 21 (13-32) |
| Patients with ARF | |
| Creatinine (μmol/L) | 260 (179-392) |
| Urea (mmol/L) | 20 (13-30) |

* APACHE II denotes Acute Physiology and Chronic Health Evaluation II, ARF acute renal failure, CRF chronic renal failure, and CRRT continuous renal replacement therapy

† Data are shown as No. (%), median (interquartile range), and mean ± standard deviation

TABLE 2. Intensive care unit admission diagnoses of all patients receiving continuous renal replacement therapy

| Diagnosis | No. of patients |
|---|---|
| Sepsis | 56 |
| Acute coronary syndrome/cardiogenic shock | 8 |
| Circulatory arrest | 7 |
| Acute renal failure (unknown cause/drug-induced) | 6 |
| Congestive cardiac failure/acute pulmonary oedema | 6 |
| Gastrointestinal perforation | 6 |
| Gastrointestinal haemorrhage | 5 |
| Pancreatitis | 5 |
| Abdominal aortic aneurysm repair | 4 |
| Electrolyte disturbance | 3 |
| Haemoptysis | 3 |
| Dissecting thoracic aortic aneurysm repair | 2 |
| Gastrointestinal ischaemia | 2 |
| Hepatorenal syndrome | 2 |
| Intracerebral haemorrhage | 2 |
| Neoplasm | 2 |
| Peripheral vascular disease | 2 |
| Burns | 1 |
| Contrast-induced nephropathy | 1 |
| Convulsion | 1 |
| Coronary artery bypass graft repair | 1 |
| Hypothermia | 1 |
| Multiple trauma | 1 |
| Pulmonary embolism | 1 |
| Retroperitoneal haematoma | 1 |
| Rhabdomyolysis | 1 |
| Ruptured hepatocellular carcinoma | 1 |

and all emergency admissions not receiving CRRT. For each group, the expected probabilities were ranked and divided into 10 sets (deciles), and the observed and expected probabilities of death were plotted.

## Results

Of 1652 ICU admissions over the 1-year audit period, 131 (8%) underwent CRRT, 20 (15%) of whom had documented CRF. Of the remaining 1632 admissions, 111 (7%) had ARF and received CRRT. In all, eight patients with ARF were readmitted and underwent additional CRRT; all such readmissions were treated as a continuation of the initial admission. The monthly period prevalence of ARF patients undergoing CRRT ranged between 4 and 12%. Overall, 56% of patients were admitted from general wards. General medicine wards were the most common source of referral (59%), followed by general surgery (18%), oncology (6%), and cardiothoracic surgery (5%) wards.

Basic patient demographics are shown in Table 1. The diagnoses of ARF and CRF patients admitted to the ICU were similar and so combined data are presented in Table 2. The mean (standard deviation) filter life was 21 (18) hours. Components used for the calculation of consumable costs included data from patients with dialysis-dependent CRF, and are summarised in Table 3. The total consumable cost per patient day for the provision of renal replacement therapy was HK$3510, which is just over one-quarter of the daily ICU bed cost of HK$13 900.[4] The durations of renal replacement therapy, ICU length of stay, ICU survival and hospital survival are summarised in Table 4. Patients undergoing CRRT had prolonged ICU stays compared to those not having such treatment (120 vs 24 hours; P<0.05), and a higher ICU mortality (38% vs 12%; P<0.05; Fig 1). Hospital mortality in the CRRT group was 53% and 20% in the non-CRRT group. Thus, receipt of CRRT was associated with a significantly increased mortality (relative risk=2.6; 95% CI, 1.9-3.6; P<0.001).

The observed hospital mortality rate in the CRRT cohort was 53%, as opposed to the 61% predicted rate from the APACHE II score, which gave an $SMR_{RA}$ of 0.86 (CI, 0.67-1.09). The observed hospital mortality rate of the patients with ARF and CRRT was 56%, which was slightly less than the 60% predicted from the APACHE II score, and gave an $SMR_{RA}$ of 0.93 (CI, 0.71-1.19). The $SMR_{RA}$ of all emergency admissions to the ICU not undergoing CRRT during the relevant period was 0.64 (CI, 0.54-0.75). The effect of CRRT on mortality adjusted for severity of illness by APACHE II is shown in Figure 2.

## Discussion

The main findings of this audit were that the percentage of patients with ARF requiring CRRT among ICU patients was high, and that they had severe illnesses and a high mortality. The disposable costs for CRRT were similar to those recently reported internationally, but the length of ICU stay of our patients having CRRT was relatively short, which was likely to reduce the overall costs per patient.

The term 'acute renal failure' was first introduced by Homer W Smith in 1951.[5] Despite common usage of the term, more than 35 different definitions have been used in the literature, creating confusion and making comparisons between studies difficult.[6] More recently, the Acute Dialysis Quality Initiative developed a renal disease classification (RIFLE).[7,8] Thus while previous single-centre studies using variable definitions reported divergent rates of ARF in ICU patients, multicentre studies using similar definitions revealed more consistent renal replacement therapy rates that ranged from 3 to 5%.[9-11] The recent multinational BEST kidney study also reported the period prevalence of ARF to be 5 to

Table 3. Cost calculation of consumables for continuous renal replacement therapy (CRRT)

| Consumables | Data |
|---|---|
| No. of patient episodes | 143 |
| No. of filters used | 564 |
| Total CRRT duration (hours) | 11 280 |
| Mean (standard deviation) filter life (hours) | 21 (18) |
| Filters used per day | 1.2 |
| Cost of filter per day (HK$850 per filter) | $1020 |
| No. of catheters used | 185 |
| Mean No. of catheters used per patient | 1.3 |
| Cost of catheter per patient (average cost of HK$328 per catheter) | $426 |
| Total amount of replacement fluid used (L) | |
| HF4 | 9567 |
| Hemosol B0 | 20 190 |
| Average amount of replacement fluid per hour (L) | 2.6 |
| Average cost of replacement fluid per day (HK$) | 2064 |
| HF4 (HK$31 per litre) | |
| Hemosol (HK$34 per litre) | |
| **Average total consumable cost for CRRT per patient day (HK$)** | **3510** |

Table 4. Summary of major outcomes*

| | All patients requiring CRRT† | ARF patients requiring CRRT† |
|---|---|---|
| Duration of CRRT (hours) | 55 (25-93) | 56 (27-93) |
| ICU length of stay (hours) | 120 (51-289) | 128 (54-299) |
| Survived to ICU discharge | 81 (62%) | 61 (55%) |
| Survived to hospital discharge | 61 (47%) | 49 (44%) |

* ARF denotes acute renal failure, ICU Intensive Care Unit, and CRRT continuous renal replacement therapy
† Data are shown in median (interquartile range) and No. (%) of patients

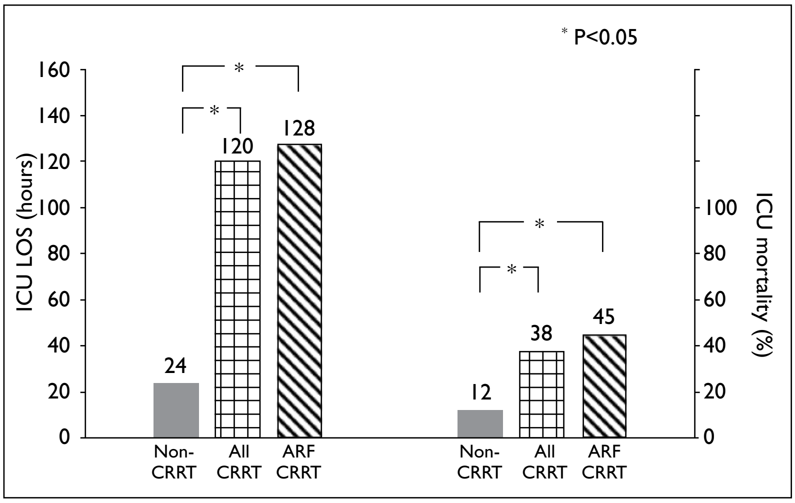


FIG 1. ICU length of stay and mortality
ICU denotes intensive care unit, LOS length of stay, CRRT continuous renal replacement therapy, and ARF CRRT acute renal failure patients with CRRT

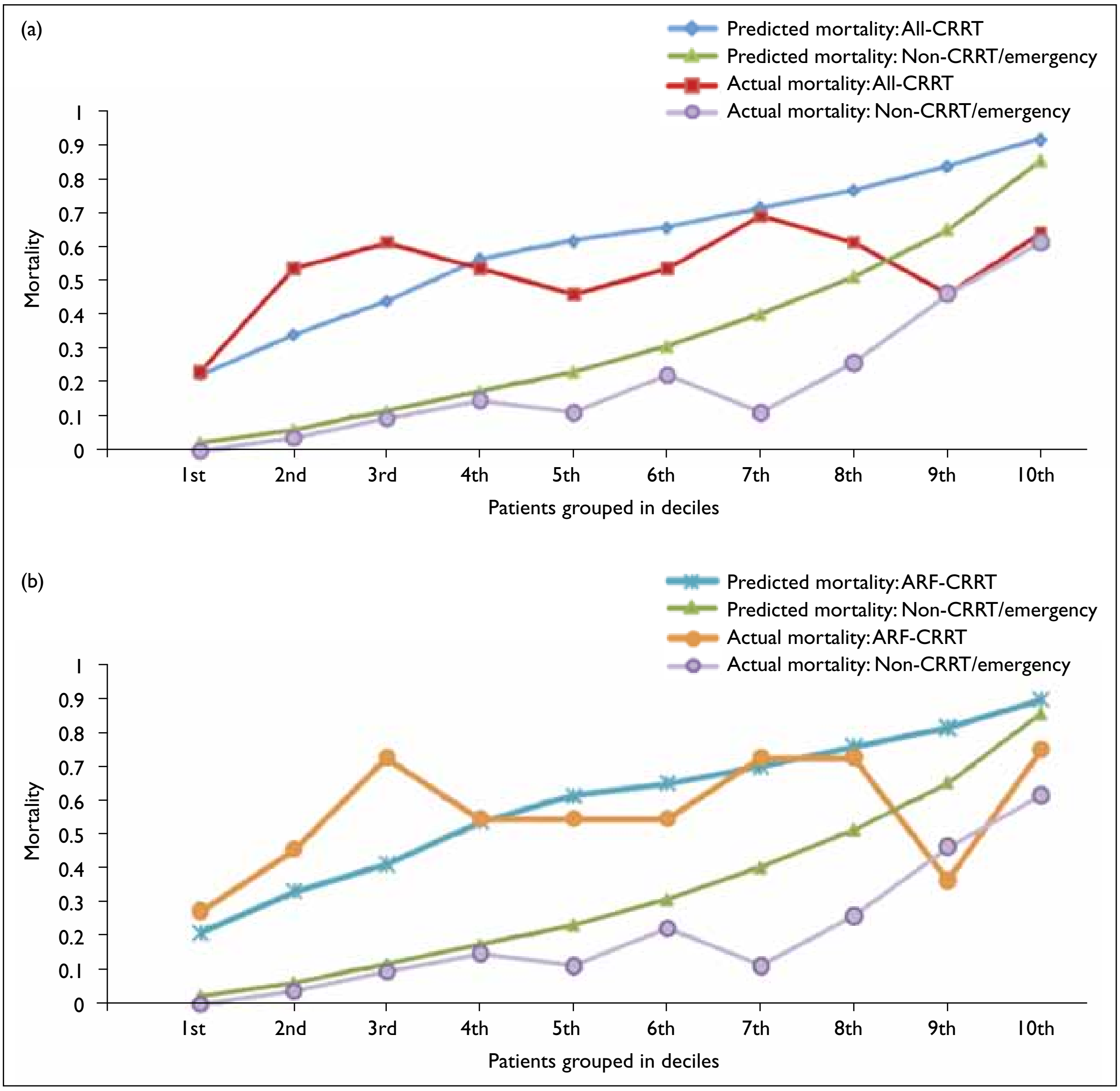


**FIG 2. Actual and predicted mortality rates for (a) all CRRT patients compared to emergency non-CRRT admissions to ICU, and (b) CRRT patients with ARF compared to emergency non-CRRT admissions to ICU**

APACHE II denotes Acute Physiology and Chronic Health Evaluation II, CRRT continuous renal replacement therapy, ICU Intensive Care Unit, and ARF acute renal failure

6%. Because of the more stringent inclusion criteria used in our audit (receipt of CRRT in addition to ARF), the period prevalence rate of 7% appears high. Specifically, the 7% CRRT in our ICU is almost double that reported in the worldwide BEST study (4%).[1] Interestingly, the only Hong Kong unit participating in this study also reported a relatively high CRRT rate. While such rates may be explained by earlier or more liberal institution of such therapy, the concentrations of urea and creatinine at the initiation of treatment were not unusually low, suggesting this explanation was unlikely.

In our cohort, 43% of the patients having CRRT had associated sepsis, which is similar to the findings of recent international studies reporting rates of 32 to 56%.[12,13]

Disposable component costs for CRRT are listed in Table 3, about which there is little information available in the literature. The major problem in conducting such an analysis was partly due to the many different modalities of CRRT available today, differences in dosing, patient variability, filter life, as well as variable equipment and disposable costs. Filter life in this study was consistent with that previously reported in other large-scale studies.[14-16] In a comparative cost analysis between CRRT and IHD, Mehta et al[17] determined both labour and disposable costs for CRRT involving continuous venovenous haemodiafiltration mode. The cost of materials (dialysate fluid, filters, and infusion pumps) was calculated to be US$338 per day.[17] From another study by Manns et al,[18] we extracted data and applied it to a total effluent rate equivalent to our use of 2.6 L/h, and estimated an equivalent cost of US$507 and Can$562 per day, respectively. Interestingly, costs of catheters used were not included in the two abovementioned studies. After excluding staff and equipment cost, it seemed that the cost of CRRT in our institution was at least as economical as that reported in international studies, particularly as discounting for time was not taken into account.

Consistent with the two previous studies, replacement and/or dialysate fluid was the main contributor to the disposable costs of CRRT, and could therefore be an appropriate target for cost-saving measures. Intuitively, although manually prepared solutions may provide potential cost reductions, recent evidence has demonstrated the contrary. When medication errors and the total costs (including acquisition costs and preparation time) were formally calculated, it was 43% more expensive than commercially available products.[19] Moreover, in a recently conducted survey of medication errors involving CRRT, 89% of them were due to manual solution preparation.[20] Other strategies, such as accurate calculation of appropriate CRRT dosage to avoid excessive solution use, may be a more efficient means of containing costs.

The median length of ICU stay of our cohort was 120 (IQR, 51-289) hours. When patients with CRF were excluded, the median length of ICU stay was 128 (IQR, 54-299) hours, which is approximately 5 days shorter than values reported internationally.[1] Recently published Hong Kong data on patients having acute renal replacement therapy in ICUs documented a median length of stay of 8 days (IQR, 4-15).[21]

Reports of ICU mortality from comparable European and North American studies ranged from 57 to 79%, and the recent multinational study of patients with ARF receiving CRRT reported a worldwide ICU mortality of 52%.[1,22-24] In Hong Kong, an ICU mortality of 54% was recently reported in a similar group of patients.[21] The lowest previously published ICU mortality of 34% was reported by Korkeila et al in a small group of 62 patients in Finland.[1,25] The ICU mortality of our cohort was also comparatively low at 38%; even when patients with CRF were excluded, it remained relatively low at 45%.

As a proportion of patients died before discharge, internationally reported hospital mortality in this group of patients was consistently higher than ICU mortality (for all patients). Nevertheless, hospital mortality has been decreasing from about 64 to 79% in the 90s[10,26-28] to about 60% cited in a more recent multicentre report.[1] Comparative data from Hong Kong showed a hospital mortality of 64%.[21] The hospital mortality in our cohort was 53%, and even when patients with CRF were excluded, the 56% rate remained comparable to internationally attained rates.

To assess the direct contribution of renal failure treated by CRRT to mortality, we adjusted observed values for the severity of illness at admission. The high $SMR_{RA}$ of patients with renal failure having CRRT compared to unselected emergency admissions, suggests that illness severity alone does not explain the high mortality in this group. The differential improvement in mortality (reduction in actual mortality compared to predicted) for patients with ARF undergoing CRRT may be larger in those with a more severe illness (Fig 2). This suggests that ICU admission and institution of CRRT may be most beneficial in this group.

The first main limitation of this audit was that it depended on information collected retrospectively from only in a single centre. Second, the indications of CRRT were not prospectively prescribed. Finally, cost data represented only disposable costs; more detailed cost analysis was not feasible due to the system of staffing, equipment procurement, and fixed cost payments prevailing in Hong Kong.

## Conclusion

Although the period prevalence of ARF patients having CRRT in the ICU was high, disposable costs were acceptable, length of ICU stays were short, and mortality relatively low compared to internationally published data, consistent with provision of a high-quality CRRT service. Nevertheless, after adjustment for severity of illness, mortality among patients who had CRRT remains higher than that observed in critically ill patients not having CRRT. Formal studies to confirm the high rate of CRRT among ICU patients in Hong Kong and determine possible causes are justified. Appropriate reductions in the use of renal replacement fluids may be an effective way of curtailing costs.

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