Nutrition and functional outcomes after critical illness due to pandemic (H1N1) 2009 influenza: a retrospective cohort study

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ABSTRACT

Objective: To determine functional outcomes 6 months after intensive care unit admission for severe infection due to pandemic (H1N1) 2009 influenza and examine the relationship between nutrition during ICU admission and outcome.

Design, setting and participants: Retrospective cohort study of patients with confirmed H1N1 influenza admitted to the ICU, Royal Adelaide Hospital, South Australia, June–October 2009.

Main outcome measures: Data were collected from medical records, dietitian notes and the daily ICU chart and included: demographics, daily kilocalories (Kcal) and protein delivered compared with dietitian-calculated requirement, ICU and hospital length of stay. Weight change and functional outcome at 6 months were determined prospectively by telephone interview using the 12-Item Short Form Health Survey and the EuroQol Group 5-Dimension Questionnaire.

Results: Of 25 patients with H1N1 infection, 23 were included in the study (14 men; median age, 48 years (interquartile range [IQR], 39–55 years); median Acute Physiology and Chronic Health Evaluation (APACHE) II score, 17 (IQR, 13–21); median ICU length of stay, 9 days (IQR, 4–15 days); median hospital length of stay, 20 days (IQR, 11–30 days); ICU mortality, 3 (13%; 95% CI, 4%–33%). Enteral feeding was commenced in 16 patients, who received a mean of 71% (SD, 27%; 95% CI, 57%–86%) of their energy and 62% (SD, 25%; 95% CI, 49%–75%) of their protein goals over their ICU stay. A more negative protein balance was associated with prolonged ICU stay ($r = -0.746$; $P = 0.003$). Reduced success of feeding was associated with increased severity of illness and shorter ICU length of stay. Patients reported a good functional outcome at 6 months.

Conclusions: Patients admitted to this ICU with H1N1 infection were fed successfully during their stay. Critically ill patients surviving H1N1 infection had good functional outcomes at 6 months.

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The global influenza A (H1N1) pandemic first emerged in Mexico in April 2009. By 6 June 2010, more than 214 countries and overseas territories worldwide had reported laboratory-confirmed cases of pandemic (H1N1) 2009 influenza, including over 18 156 deaths.[1] In the Southern Hemisphere, the pandemic coincided with the winter season, resulting in a greater impact on health services compared with the experience of the Northern Hemisphere. Between 1 June and 31 August 2009, 722 patients were admitted to an intensive care unit in Australia or New Zealand with confirmed H1N1 influenza.[2] Infants (aged under 1 year) and adults between the ages of 25 and 64 years were found to be at particular risk. As the patients affected by this pandemic were a relatively young population, their recovery and functional outcome is of great interest. However, the functional recovery of patients admitted to hospital with severe H1N1 influenza during the pandemic of 2009 has not yet been reported in the medical literature. This is important, as H1N1 infection continues to affect health care resources worldwide.[3]

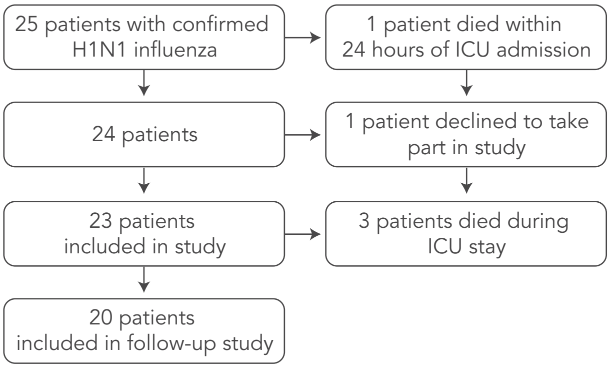
Early enteral nutrition is considered best practice for patients admitted to ICU.[4,5] Negative energy balances during ICU stay have been shown to correlate with increased complications, particularly infections.[6] Greater success of energy and protein delivery throughout ICU stay has also been associated with improved outcomes among critically ill patients.[7] However, despite early enteral nutrition being shown to decrease hospital mortality,[8] the relationship between energy and protein delivery during ICU stay and functional outcomes after ICU discharge is unclear. It is likely that weight loss and muscle wasting frequently seen after critical illness will result in delayed functional recovery, but this has not been formally quantified.

We assessed the functional outcome of a cohort of patients admitted to an Australian ICU with severe H1N1 influenza. We also examined the relationship between nutrition during ICU stay and functional and nutritional outcomes after discharge.

Methods

A retrospective cohort study was performed at the 34-bed adult general ICU of the Royal Adelaide Hospital, South Australia. All patients admitted to the ICU between June

Figure 1. Enrolment of patients with confirmed H1N1 influenza, Royal Adelaide Hospital intensive care unit, June–October 2009



and October 2009 with H1N1 influenza infection, confirmed by polymerase chain reaction (PCR) assay, were identified for inclusion. Institutional ethics committee approval was obtained for this study (protocol no. 091111). Patients were given the opportunity to opt out of the study in writing before initial telephone contact. Patients were excluded if they died within 24 hours of ICU admission (Figure 1).

Data were collected from patient case notes and ICU charts for the period of ICU stay, to a maximum of 30 days from ICU admission. Data collected included: patient demographics; Acute Physiology and Chronic Health Evaluation (APACHE) II score and diagnosis; date and time of admission to and discharge from ICU and hospital; ICU and hospital survival; and use of mechanical ventilation, non-invasive ventilation, vasopressor therapy and renal replacement therapy.

Data were collected on patients' nutritional status, including: weight on admission to ICU and during hospital stay; height; date and time of initiation of enteral feeds; type of feeds; volume of feeds delivered; volume of gastric aspirates and use of parenteral nutrition. Daily energy delivery was measured and compared with requirements calculated by the ICU dietitian using the Schofield equation. Protein delivery was compared with protein requirements, calculated as 1.2–1.5 g/kg/d. Adequacy of nutrition was defined as the percentage of energy and protein delivered compared with the goal for each patient. Cumulative energy and protein balance were then calculated.

Follow-up of patients was undertaken at 6 months after admission to ICU. A telephone interview was conducted using standardised assessment tools; the 12-Item Short Form Health Survey (SF-12v2) and the EuroQol Group 5-Dimension Questionnaire (EQ-5D) to measure health-related quality of life and health outcomes. Nutritional follow-up involved completion of a questionnaire based on the Patient-Generated Subjective Global Assessment (PG-SGA) collecting information on weight, oral intake, symptoms affecting eating and dietary supplementation. These questionnaires were sent to patients before the telephone interview for their reference.

Table 1. Characteristics of 23 patients admitted to ICU with H1N1 influenza

Characteristic	
Sex, no.	
Male	14
Female	9
Median age in years (IQR)	48 (39–55)
Median BMI (IQR)	32 (27–37)
Median APACHE II score (IQR)*	17 (13–21)
APACHE II diagnosis, no.*	
Cardiogenic shock	1
Respiratory infection	21
Hospital survival, no.	
Died	3
Survived	20
ICU survival, no.	
Died	3
Survived	20
Median hospital length of stay in days (IQR)	20 (11–30)
Median ICU length of stay in days (IQR)	9 (4–15)

IQR = interquartile range. BMI = body mass index. APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intensive care unit.
* APACHE data were missing for one patient.

Table 2. Patient interventions (*n* = 23)

	Patients
Mechanical ventilation	17
Non-invasive ventilation	2
Renal replacement therapy	2
Vasopressor therapy	13
Extracorporeal membrane oxygenation	1

Descriptive data are shown as median (interquartile range [IQR]) or mean (SD), with 95% confidence intervals given where appropriate. Relationships between feeding measures and APACHE II score, ICU and hospital length of stay and weight change were assessed using Pearson correlations. Non-parametric Mann–Whitney tests were used to test for differences in feeding measures according to ICU and hospital outcome. SPSS, version 18 (IBM, Armonk, NY, USA) was used for all analyses. Statistical significance was defined as $P < 0.05$.

Figure 2. Percentage of energy and protein goals delivered per day of intensive care unit stay

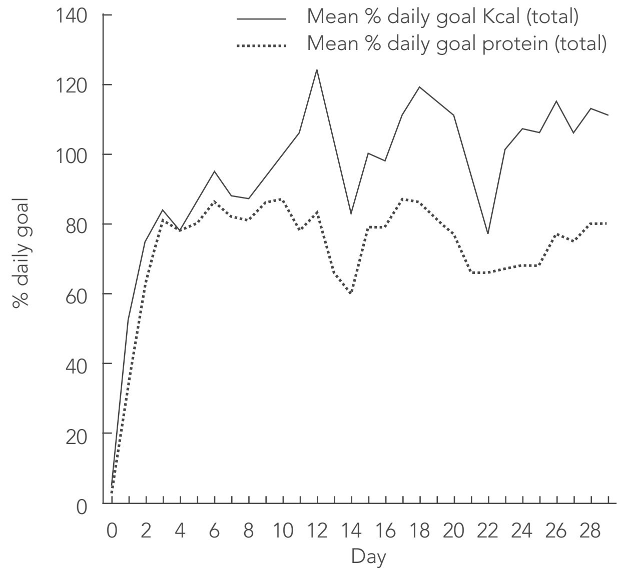


Figure 3. Correlation between mean percentage total energy delivered and intensive care unit length of stay ($r = 0.797$; $P = 0.001$)

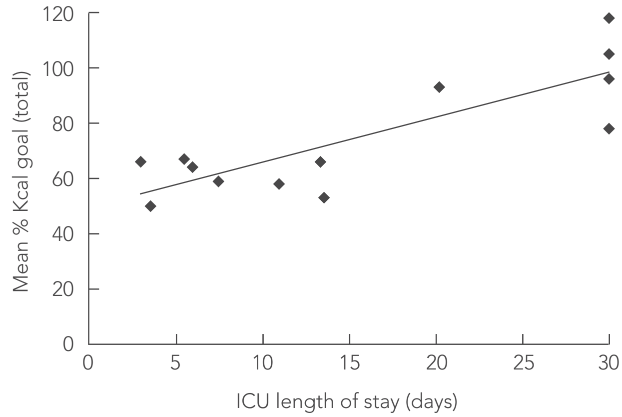
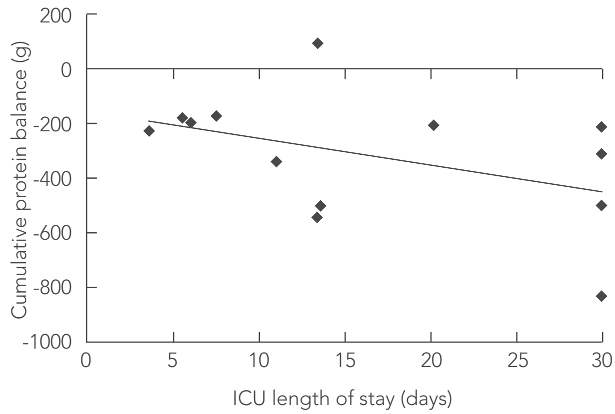


Figure 4. Correlation between cumulative protein balance and intensive care unit length of stay ($r = -0.746$; $P = 0.003$)



Results

From 17 June to 14 October 2009, 25 patients were admitted to the Royal Adelaide Hospital ICU with 2009 H1N1 influenza. Twenty-three patients were included in the analysis (Figure 1). Patient characteristics are shown in Table 1. Patient interventions are illustrated in Table 2.

Enteral feeding was commenced for 16 patients at a median of 14 hours (IQR, 9–27 hours) after admission to the ICU. One patient was mechanically ventilated but did not receive enteral feeding. One patient received parenteral feeding for 1 day in addition to enteral feeding.

Median daily nutritional requirements were calculated as 1800 Kcal/d (IQR, 1750–2025 Kcal/d) and 96 g/d (86–102 g/d) of protein. Patients received a mean daily enteral feeding volume of 1061 mL (SD, 417 mL; 95% CI, 839–1283 mL). This provided a mean of 66% (SD, 25%; 95% CI, 52%–79%) of the calculated energy goals and 62% (SD, 25%; 95% CI, 49%–75%) of the protein goals over the course of their ICU stay. When propofol and parenteral nutrition were included in the calculations, patients received a mean of 71% (SD, 27%; 95% CI, 57%–86%) of their energy goal requirements. Figure 2 shows the daily percentage of energy and protein goals delivered. Mean cumulative energy balance over ICU stay was – 4003 Kcal (SD, 4761 Kcal; 95% CI, – 6540 to – 1466 Kcal). Mean cumulative protein balance over ICU stay was – 415 g (SD, 393 g; 95% CI, – 624 to – 205 g).

Six patients who received enteral feeding required prokinetic therapy within the first 72 hours of admission due to large gastric residual volumes (38%; 95% CI, 18%–61%), and 10 patients had one or more gastric aspirates greater than 250 mL during enteral feeding (63%; 95% CI, 39%–82%). Three patients had postpyloric feeding tubes inserted after continued feeding difficulties despite prokinetic therapy.

Patients who had a longer ICU stay received a greater percentage of goal calories enterally ($r = 0.795$; $P = 0.001$) and in total including propofol and parenteral nutrition ($r = 0.797$; $P = 0.001$) (Figure 3), and had a more negative total protein balance ($r = -0.746$; $P = 0.003$) (Figure 4).

Increased illness severity as demonstrated by a higher APACHE II score was associated with reduced feeding success (Table 3). There was no correlation between feeding and ICU or hospital mortality.

Twenty patients were included in the 6-month follow-up (Figure 1). Sixteen patients reported good to excellent general health at follow-up (80%; 95% CI, 58%–92%).

Table 3. Correlations between feeding and APACHE II score ($n = 16$)

	r	P
Mean daily volume of enteral feeds, mL	– 0.692	0.002
Per cent goal Kcal enteral	– 0.626	0.007
Per cent goal protein enteral	– 0.737	0.001
Per cent goal Kcal total	– 0.619	0.008

APACHE = Acute Physiology and Chronic Health Evaluation.

However, 13 patients reported they were limited by their health in moderate or strenuous activities (65%; 95% CI, 43%–82%) (Figure 5). The impact of patients' physical and emotional health on their ability to accomplish what they would have liked is illustrated in Figure 6. Nine patients required family members to care for them after discharge from hospital (45%; 95% CI, 26%–66%) for a median of 18 days (IQR, 14–60 days). None of the participants required a paid carer. Relatives of one patient took time off work to care for them. Six patients had re-attended an emergency department since discharge from hospital, mostly with unrelated illnesses or injuries (30%; 95% CI, 14%–52%). One patient had been readmitted to the ICU during the follow-up period.

Nine patients (45%) were working before admission to the ICU. At 6 months, six had resumed their normal type and hours of work (30%; 95% CI, 14%–52%). One patient was working fewer hours than previously (5%; 95% CI, 0–25%), and two patients had stopped working (10%; 95% CI, 2%–31%).

The median weight pre-ICU admission was 90 kg (IQR, 85–100 kg). Median weight change during ICU stay was – 1.5 kg (– 7.3 to + 0.8 kg) and cumulative weight change at 6 months was – 1.3 kg (– 6.0 to + 2.3 kg) based on patient estimated weight. Two patients were taking vitamin supplements, but none required other dietary supplementation at follow-up.

Overall, patients reported a median visual analogue scale (VAS) wellness score of 80 (IQR, 58–90) before their illness with H1N1 influenza and admission to ICU. This had fallen to 71 (IQR, 50–85) at 6 months. The median change in VAS wellness score pre- to post-ICU admission was 0 (IQR, – 9 to 0). There was no correlation between feeding success during ICU stay and functional outcomes at 6-month follow-up.

Figure 5. Impact of health on ability to perform moderate activities (eg, moving a table) and strenuous activities (eg, climbing several flights of stairs) at 6 months

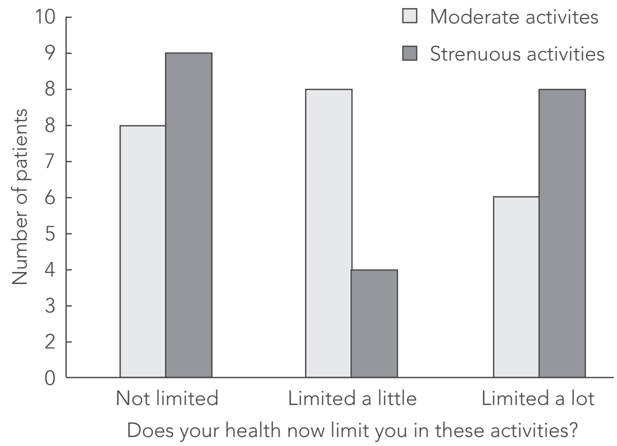
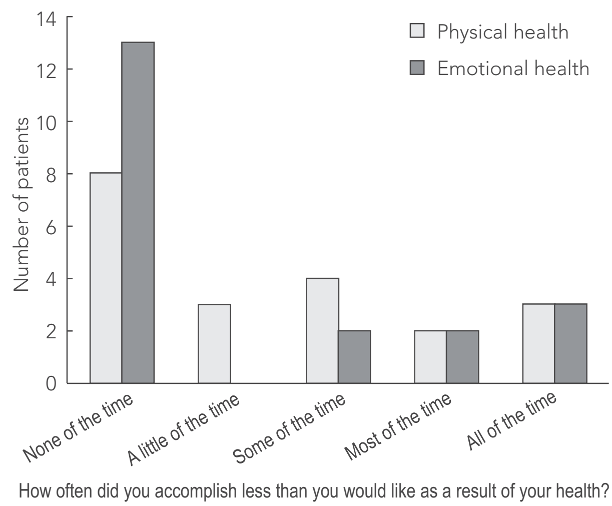


Figure 6. Impact of physical and emotional health on ability to accomplish goals at 6 months



Discussion

To our knowledge, this is the first study to demonstrate good functional outcomes 6 months after ICU admission in patients with severe H1N1 influenza. Furthermore, although overall nutrition during ICU stay did not appear to influence functional outcomes at 6 months, patients who stayed in ICU longer had increased energy and reduced protein intake. Weight loss over the ICU stay was modest but persisted for at least 6 months.

The cost of intensive care varies according to the interventions required, but has been estimated to be around AUD$3416–$3787 per day (2555–2832 Euros).[9] As the cost of intensive care treatment is high, it is important to be able to demonstrate good functional outcomes and quality of life after discharge. Functional outcome after H1N1 influenza infection is of particular interest, as relatively young people appear to be affected.[2]

The results of our study suggest that the provision of intensive care to patients with severe H1N1 infection usually results in a good functional outcome. All patients who survived to ICU discharge were alive at 6-month follow-up. Functional outcome at 6 months was assessed using the EQ-5D and SF-12 health outcomes questionnaires, which have been extensively used in the medical literature and have been validated for use across a range of disease states.[10-14] Overall, patients reported a good functional outcome. Most patients limited in moderate or strenuous activities at follow-up reported this to be pre-existing before ICU admission; however, some had experienced a deterioration of their previous problems. Despite the reported good functional outcomes, over 20% of patients who were working before ICU had not returned to work at 6 months. This has potential economic ramifications for patients, their families and society. Several patients who were limited most or all of the time by their physical health also reported being limited by their emotional health.

The provision of only two-thirds of the calculated energy and protein goals over the course of their ICU stay is consistent with numerous other studies.[7,15-19] This occurred despite our ICU's policy of providing nutritional support according to a nutrition guideline. This guideline recommends early initiation of enteral feeding and intervention with pro-motility agents and small intestinal delivery when feeding is unsuccessful. Despite a median time of just 14 hours from admission to commencing feeds, it took 72 hours for patients to be receiving 80% of their estimated daily requirement of protein and energy. This delay in achieving full delivery of enteral nutrition has been reported previously,[7] and contributes to a cumulative energy deficit that develops over the ICU stay.[6]

There are several reasons for the delay in meeting nutritional requirements. Some patients were not invasively ventilated immediately on arrival to the ICU and instead had a trial of non-invasive ventilation, which requires a period of fasting before intubation. There was also a relatively high rate of feed intolerance in our study population (63% of patients had at least one gastric aspirate greater than 250 mL during feeding). Feed intolerance is usually observed in about 50% of critically ill patients,[15,20,21] and commonly occurs within the first few days of feeding. Six patients required prokinetic therapy and a reduction in feeding rate due to large gastric aspirates within the first 72 hours after commencement of enteral feeding. It has been suggested that treating large gastric residual volumes with prokinetic agents and continuing feeding at the same rate may be safe and avoid the energy deficit that develops early in the ICU stay.[22]

Reasons for reduced success of feeding in this group are likely to be multifactorial, but include severity of illness as demonstrated by the relationship between APACHE II score and reduced energy delivery.

We found a positive relationship between ICU length of stay and increased energy delivery. Although the relationship between length of ICU stay and energy delivery could reflect increased complications caused by increased energy delivery (overfeeding), it is also possible that this association is due to the increased success of feeding as patients stay longer in the ICU. The largest energy deficit was present during the first 72 hours of ICU stay — by Day 10, patients were receiving 100% of their estimated daily energy requirement.

Despite the positive relationship between ICU length of stay and energy delivery, a negative relationship existed between ICU length of stay and total protein balance. Again, although it is easy to understand how a cumulative protein deficit may be associated with prolonged ICU stay and poor outcomes, the observed association may be due to the fact that the percentage of daily goal protein delivered never rose above 87% (Day 10 and Day 17). Thus, the longer patients stayed in ICU, the bigger protein deficit they accumulated. The association between protein deficit and prolonged ICU stay therefore needs to be interpreted with caution.

The calories delivered by propofol were also relevant to feeding success. Propofol delivers 1.1 Kcal/mL,[23] but does not contain protein. During a 28-day ICU stay, one patient received 5000 mL of propofol, equating to 5500 Kcal. Calories delivered by propofol may in part account for the difference in the success of energy delivery compared with protein delivery.

Our study was a single-centre retrospective analysis, and was limited by the small number of patients admitted with H1N1 influenza. As data were collected retrospectively, the study was also limited by the quality of data already recorded. This is particularly relevant when considering patient weights, which were generally determined by patient history or dietitian estimate. Although this is standard practice in ICU management, it makes interpretation of change in weight over time potentially inaccurate. Weight is rarely measured in ICU patients due to practical difficulties. Weight loss in this moderately obese group of patients was modest at 1.5 kg over the ICU stay.

Although the small sample size may limit the translation of these results to other units, there is no reason to believe that these outcomes would not reflect functional and nutritional outcomes following ICU admission for H1N1 infection in other centres in the Western world. As further waves of H1N1 influenza put strain on critical care resources this information will be particularly valuable.

In conclusion, functional outcome was generally good after ICU stay for H1N1 infection in this Australian cohort. Enteral nutrition was delivered successfully and weight loss was minimal.

Competing interests

None declared.

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