It's time to optimise dosing of unfractionated heparin in obese patients

Christopher George[1,2]*, Karl Winckel[1,2], Dr Michael Barras[1,2], Judith Coombes[1,2], Dr Neil Cottrell[1]

[1]School of Pharmacy, The University of Queensland, Pharmacy Australia Centre of Excellence, Brisbane, QLD, Australia

[2]Pharmacy Dept, Princess Alexandra Hospital, Brisbane, Queensland

*christopher.george@health.qld.gov.au

Introduction

Obesity (BMI ≥ 30kg/m²) has a prevalence of approximately 30% within the Australian adult population, and is predicted to increase by 0.8% per year.[1, 2] Obesity is a major risk factor for a number of embolic disorders such as Acute Coronary Syndromes (ACS) and Venous Thromboembolism (VTE).

Unfractionated Heparin (UFH) is an anticoagulant frequently used for treatment of VTE and ACS. Concerns regarding its use include bleeding and risk of clot extension. In non-obese individuals UFH has a reported Volume of Distribution (Vd) similar to that of blood volume.[3] Obesity is associated with an increase in blood volume and subsequently Vd, therefore obese patients require greater doses of IV UFH.[4]

In proportion to lean tissue, adipose tissue contains little vasculature, leading to variable distribution of UFH throughout the body.[4] Due to this, conservative dose capping of UFH in obese patients is a current practice used to reduce the risk of bleeding (Figure 1).[5]
UFH is monitored using Activated Partial Thromboplastin Time (APTT). Within Queensland Health (QH), therapeutic APTT ranges are indication specific; 71-100 seconds for ACS/bridging therapy and 71-110 seconds for VTE.

There is concern that conservative dose capping leads to subtherapeutic APTTs.

Figure 1: Queensland Health Unfractionated Heparin Dosing Nomogram v11

Indication	Initial bolus	Initial Infusion rate
Warfarin Therapy Replacement or Acute Coronary Syndrome	**60 units/kg** (with thrombolytic: max 4 000 units no thrombolytic: 5 000 units)	**12 units/kg** (for weight < 84kg) (max 1 000 units/hr)
Acute Treatment of Pulmonary Embolisom or Deep Vein Thrombosis	**80 units/kg** (max 8 000 units)	**18 units/kg/hr** (for weight < 84kg) (max 1 500 units/hr)
For specialist surgical indications refer to medical Officer or unit specific protocols		

Aim

To determine what maintenance doses of unfractionated heparin (UFH) result in a therapeutic APTT in patients with increasing levels of obesity.

Methods

Using the QH Electronic Medical Record (iEMR), the medical records of identified patients were retrospectively reviewed at the Princess Alexandra Hospital (PAH). After identification patients were grouped into total body weight (TBW) cohorts of either; <100kg (non-obese), 100-124.9kg, 125-150kg or >150kg. Patient baseline characteristics (weight, height, smoking status, co-morbidities and ethnicity) were noted. Both electronic and paper heparin orders were analysed, with all doses and corresponding APTTs recorded until 2 consecutive therapeutic APTTs were reached. The dose at this point was determined as the required dose for that patient. For patients not reaching 2 consecutive therapeutic APTTs, dosing requirements were unable to be estimated. These patients were excluded from the analysis.

Results

Throughout the study period a total of 113 patients were analysed. These patients were broken down and analysed by weight cohorts (figure 2).

Our data demonstrated that as weight increased so did the requirements for absolute (total units) UFH infusion dose (figure 3). However, this is not proportional to weight-based (u/kg) infusion doses (figure 4). This reflects obese physiology where adipose tissue has little influence on the pharmacokinetics of UFH.

A significantly greater number of obese patients required infusion doses above the initial dose-capped recommendation to attain a therapeutic APTT when compared to the < 100kg cohort (p = 0.0047).

Figure 2: Patient recruitment and analysis flowchart

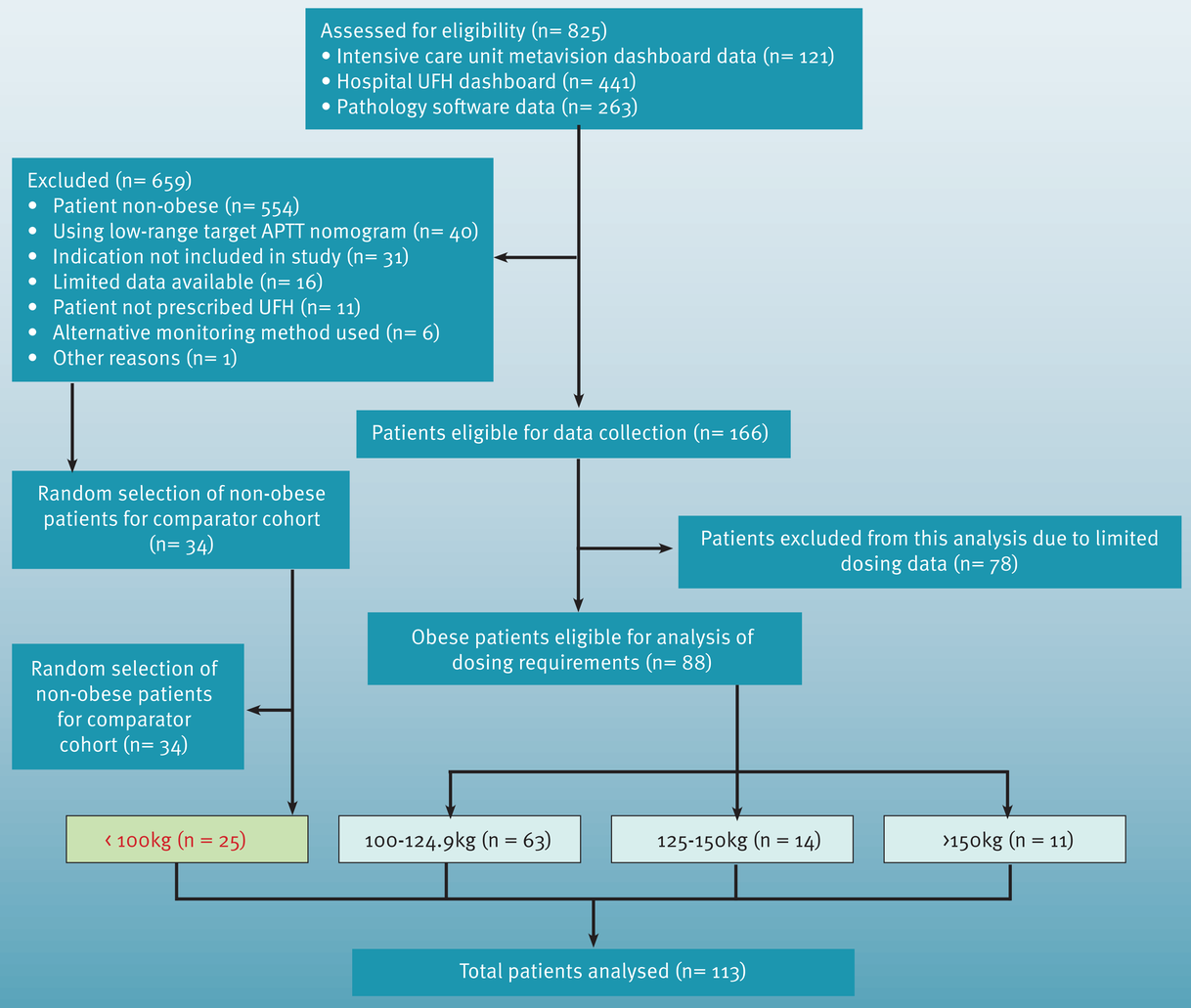


Figure 3: mean ± standard deviation absolute infusion dose (u/hr) required to achieve 2 consecutive therapeutic APTTs

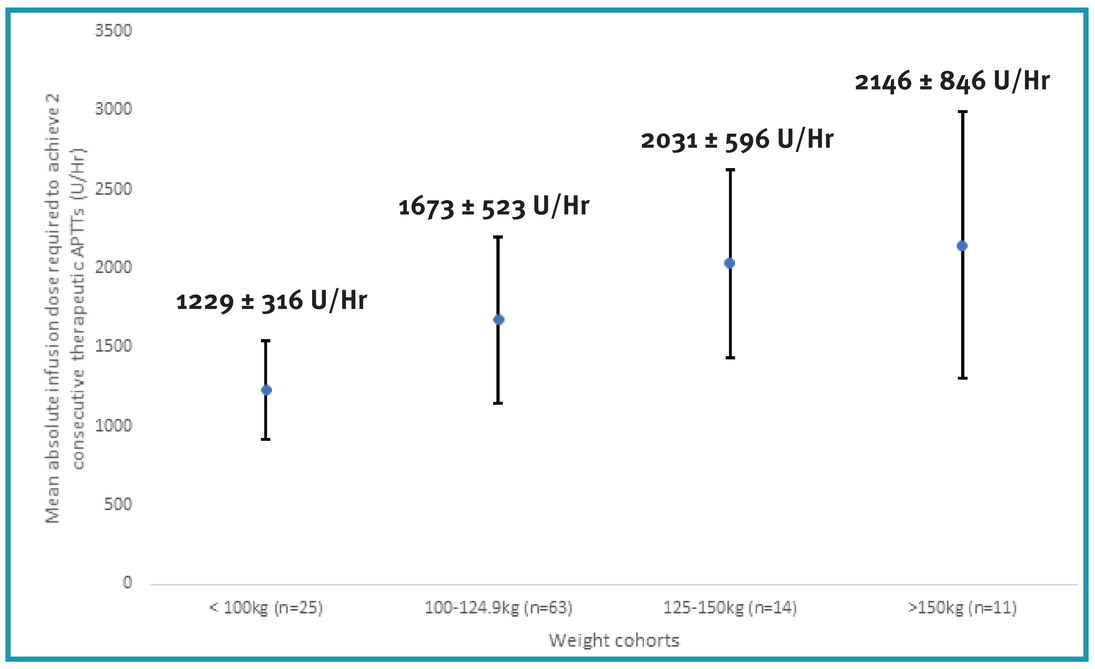


Figure 4: mean ± standard deviation weight based infusion dose (u/kg[TBW]/hr) required to achieve 2 consecutive therapeutic APTTs

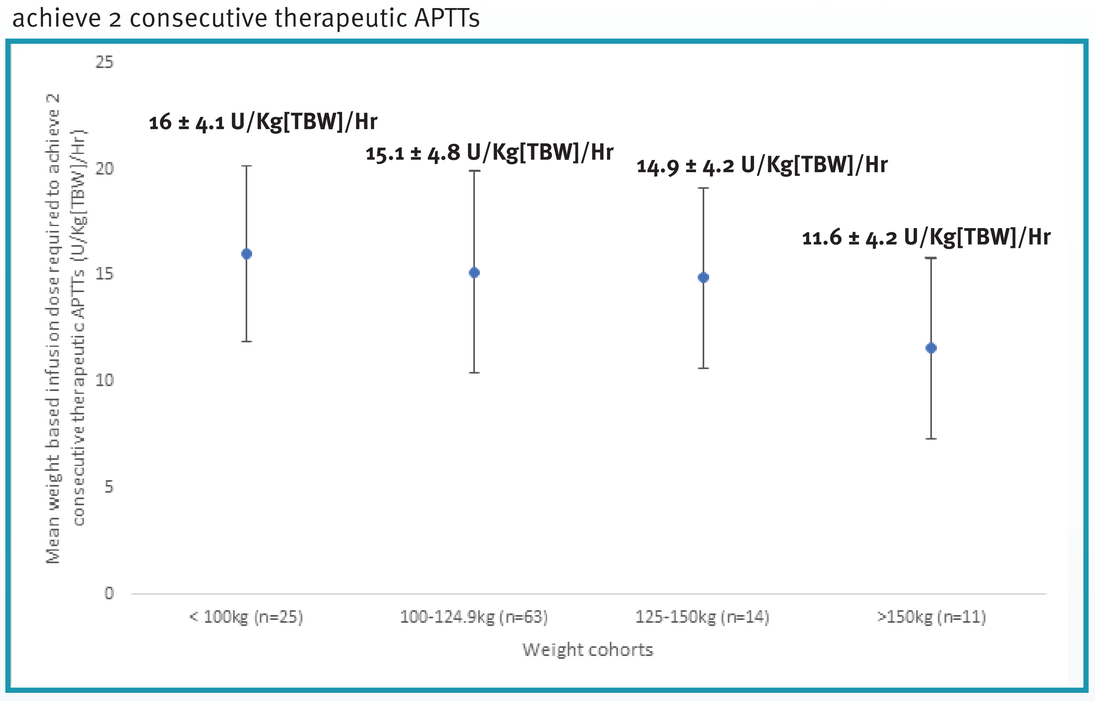
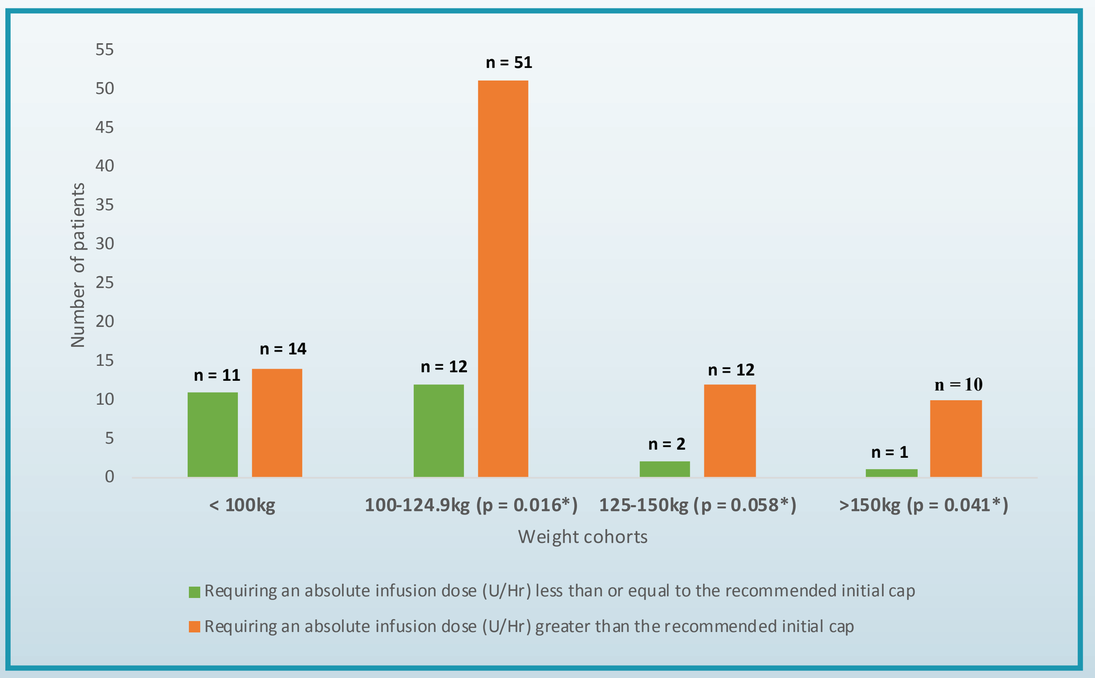


Figure 5: Number of patients whose initial capped infusion dose was adequate or inadequate



Conclusion

Larger absolute doses (U/Hr) of IV UFH should be considered in obese patients. However, these doses should be based on reduced and uncapped TBW (U/Kg[TBW]/Hr).
Our results support published studies where 14.6Units/kg(TBW)/hr, 13Units/kg(TBW)/hr and 11.3Units/kg(TBW)/hr are recommended for 100-124.9kg, 125-150kg, and >150kg patients respectively. It is likely that using a similar dosing regimen in a QH setting would produce rapid attainment of APTT, producing the associated beneficial outcomes for patients.

References

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