

Challenges in determining renal function and dosing in a transgender patient receiving carboplatin/etoposide chemotherapy

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Clinical Features

- A 64 year old transgender woman presented with obstructive nephropathy and renal impairment secondary to newly diagnosed urothelial carcinoma (predominantly small cell type).
- Chemotherapy treatment was delayed due to urinary tract infections, pulmonary emboli (PE) and ureteric stent blockage (nephrostomy remaining in-situ).
- Prescribed estradiol hormone therapy since gender affirming surgery in 1993.
- Potential CYP450 drug interactions between concurrent medications and proposed chemotherapy identified.

Literature Review

- Limitations on estimating glomerular filtration rate (GFR) using standard equations in this patient cohort were identified.¹
- Limited data is available on the effects of hormone therapy on renal clearance and ideal body mass in transgender patients.^{1,2,3}
- Measured GFR is considered the gold-standard assessment as not dependent on sex or muscle mass;² however, was not suitable whilst nephrostomy in situ.
- Data suggests the physiology of transgender patients receiving hormone therapy for more than 6 - 12 months should resemble cisgender patients of their gender identity.¹

Dosing Considerations			
Effects of hormone therapy?	How to assess GFR?	Impact of clinical history?	Chemotherapy dosing formulas?
<p>On body mass / body surface area (BSA):</p> <ul style="list-style-type: none"> - Differences in fat, muscle and plasma volume of distribution between genders = effects of hormone therapy on this unknown.¹ - Biometric measures seen to more closely measure gender identity than sex at birth in transgender women after prolonged hormone therapy.¹ <p>On renal clearance:</p> <ul style="list-style-type: none"> - Serum creatinine is produced from muscle metabolism. - Effects of gender affirming doses of hormone therapy on renal function to be determined.³ 	<p>a) Measured GFR:</p> <ul style="list-style-type: none"> - Gold standard - Not dependent on sex or muscle mass - Limited by availability and patient suitability. <p>b) Estimated GFR using:</p> <ul style="list-style-type: none"> - Cockcroft Gault formula (CG) vs Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI) - Both require sex and muscle mass for calculation - Unclear if creatinine based equations reliably estimate kidney function in transgender patients on hormone therapy.³ 	<p>Medical complications:</p> <ul style="list-style-type: none"> - Urinary tract infections (<i>Escherichia coli</i> & <i>Candida glabrata</i>) - Bilateral PE - Right ureteric stent blockage requiring nephrostomy - Renal impairment and fluctuating creatinine - CYP450 interactions identified with concurrent fluconazole, apixaban and proposed etoposide chemotherapy = may increase risk of toxicity. 	<p>Weight calculated using:</p> <ul style="list-style-type: none"> - Actual weight vs Ideal body weight vs Adjusted ideal - Actual weight normally used for dose calculation.⁴ <p>Etoposide dose calculated using:</p> <ul style="list-style-type: none"> - BSA = Dubois Dubois vs Mosteller formulas - Dose adjusted based on renal and/or hepatic function.⁵ <p>Carboplatin dose calculated using:</p> <ul style="list-style-type: none"> - Calvert formula: Dose (mg) = AUC x (25 + GFR)⁶ - Dose calculation directly correlated to renal function.
<p>Challenge #1 Assessing impact of withholding estradiol for 4 weeks (due to new PE) in light of overall duration of therapy (since 1993).</p>	<p>Challenge #2 Estimating renal function in a transgender patient without access to direct GFR measurement (nephrostomy in-situ).</p>	<p>Challenge #3 Optimising treatment efficacy, whilst minimising risk of toxicity arising from comorbidities and drug interactions.</p>	<p>Challenge #4 Determining most appropriate weight and creatinine values to use in required dosing formulas/calculations.</p>
<p>Clinical assessment: Review of estimated GFR formula, weight and creatinine with clinical history to determine chemotherapy doses and recommended monitoring required</p>			

Evaluation/Recommendations

Carboplatin dose:

- 24 dosing scenarios were modelled based on variables in GFR estimation:
 - ❖ *Estimated GFR formula:* CG (Figure 1) or CKD-EPI (Figure 2)
 - ❖ *Gender:* Female (F) or Male (M)
 - ❖ *Serum creatinine levels:* 145 µmol/L or 167 µmol/L (fluctuating)
 - ❖ *Body weight:* Actual, Ideal or Adjusted ideal.
- Calculated values using female-based equations included:
 - ❖ *Estimated GFR:* 28mL/min to 44mL/min (37% difference)
 - ❖ *Carboplatin dose:* 270mg to 345mg (22% difference).
- Treatment dose (= 285mg) was calculated using:
 - ❖ Calvert formula (AUC 5) per chemotherapy protocol.⁵
 - ❖ CKD-EPI formula to estimate GFR (adjusted to BSA).⁶
 - ❖ Female gender
 - ❖ Actual body weight
 - ❖ Dubois Dubois formula to calculate BSA
 - ❖ Highest creatinine (167 µmol/L).

Etoposide dose:

- Treatment dose was calculated using:
 - ❖ Actual body weight
 - ❖ Dubois Dubois formula to calculate BSA.
- 25% dose reduction was applied due to renal impairment as per chemotherapy protocol guidelines (GFR 30-50mL/min).⁶

Rationale:

- Extended duration of prior estradiol therapy
- To minimise risk of treatment toxicity due to infection risk and drug interactions

Conclusion

- ➡ This case highlights the complexity in medication dosing and assessment of GFR in transgender patients with renal impairment.
- ➡ Significant role for the pharmacist in literature review, drug interaction assessment, dose calculations and patient education to optimise treatment efficacy, minimise toxicity and provide holistic care in this patient cohort.
- ➡ Further research into the effects of hormone therapy on body mass and renal function in this patient population is warranted to guide future practice.

References

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Figure 1: Estimated GFR and Carboplatin Dose (CG formula)

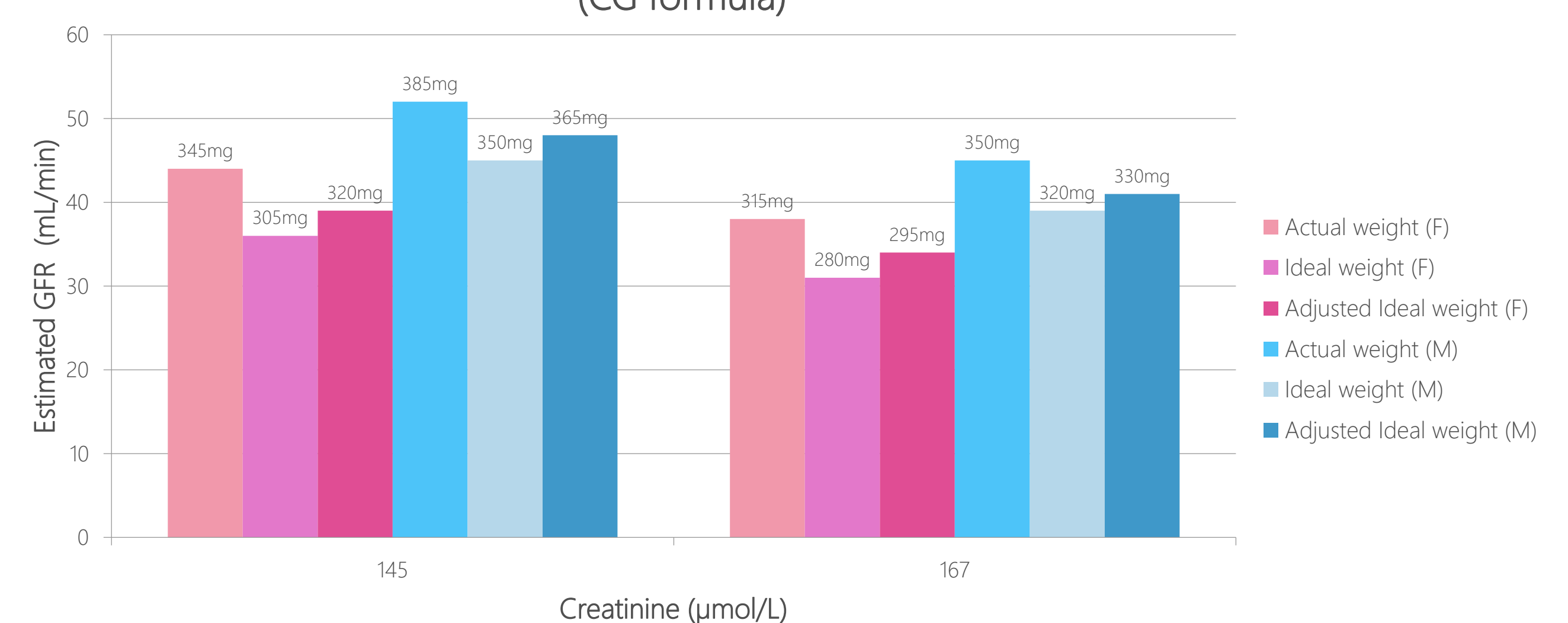


Figure 2: Estimated GFR and Carboplatin Dose (CKD-EPI formula)

