



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Xu, Y;Testro, A;Wong, A

Title:

Analysis of the Australia and New Zealand referral criteria for transfer to a liver unit for paracetamol overdose

Date:

2021-12-01

Citation:

Xu, Y., Testro, A. & Wong, A. (2021). Analysis of the Australia and New Zealand referral criteria for transfer to a liver unit for paracetamol overdose. *EMA Emergency Medicine Australasia*, 33 (6), pp.1021-1026. <https://doi.org/10.1111/1742-6723.13795>.

Persistent Link:

<https://hdl.handle.net/11343/298532>

Analysis of the Australian New Zealand referral criteria for transfer to a liver unit for Paracetamol Overdose

Short: Paracetamol OD ANZ criteria referral

Corresponding Author (Final author) and Senior Author:

Associate Professor Anselm Wong PhD

Department of Critical Care, University of Melbourne and Emergency Department, Austin Health, Victoria, Australia.

Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.

Address: Emergency Department, Austin Hospital, Studley Road, Heidelberg, Victoria 3084, Australia.

Email: anselm.wong@austin.org.au

Tel: +61394964509

Co-authors:

Dr Joyce Xu (1st author)

Melbourne Medical School, University of Melbourne
Melbourne, Australia

A/Prof Adam Testro (2nd author)

Liver Transplant Unit
Austin Health
Heidelberg
Victoria, Australia

Conflicts of interest: Nil to declare.

Contribution: JX drafted the case report. All authors contributing to editing and writing the manuscript.

Funder: AW is supported by a NHMRC Research Fellowship ID 1159907

Word count: 2253

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/1742-6723.13795](https://doi.org/10.1111/1742-6723.13795)

This article is protected by copyright. All rights reserved.

Analysis of the Australian New Zealand referral criteria for transfer to a liver unit for Paracetamol Overdose

Short: Paracetamol OD ANZ criteria referral

Corresponding Author (Final author) and Senior Author:

Associate Professor Anselm Wong PhD

Department of Critical Care, University of Melbourne and Emergency Department, Austin Health, Victoria, Australia.

Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.

Address: Emergency Department, Austin Hospital, Studley Road, Heidelberg, Victoria 3084, Australia.

Email: anselm.wong@austin.org.au

Tel: +61394964509

Co-authors:

Dr Joyce Xu (1st author)

Melbourne Medical School, University of Melbourne
Melbourne, Australia

A/Prof Adam Testro (2nd author)

Liver Transplant Unit
Austin Health
Heidelberg
Victoria, Australia

Conflicts of interest: Nil to declare.

Contribution: JX drafted the case report. All authors contributing to editing and writing the manuscript.

Funder: AW is supported by a NHMRC Research Fellowship ID 1159907

Word count: 2253

ABSTRACT

Objectives

Paracetamol overdose is common and can lead to fulminant hepatic failure. In cases that are not improving with standard medical therapy with N-acetylcysteine, some patients may require liver transplant. The Australia and New Zealand (ANZ) referral criteria for transfer to a liver unit has not been extensively studied for its predictive value. The aim of this study was to evaluate the ANZ referral criteria for predicting mortality in paracetamol overdose.

METHODS

This study involves a retrospective analysis of patients who developed hepatotoxicity post paracetamol overdose presenting to an Australian health service with a liver transplant unit between 2010 and 2019 and were treated with N-acetylcysteine. The primary outcome was death or transplant.

RESULTS

Out of 983 paracetamol overdose presentations, 81 (8.2%) cases developed hepatotoxicity. Of these, 17 cases (21%) met the composite endpoint of death or transplant. The ANZ referral criteria is highly sensitive at predicting the primary endpoint of death or transplant at time of referral 100% (95%CI: 81, 100) but had low specificity at 30% (95%CI: 19, 42).

CONCLUSIONS

The ANZ referral criteria was highly sensitive for predicting the outcome of mortality and transplant. This is important for screening patients that may become unstable and difficult to transfer at a later stage of their admission.

Keywords: acetaminophen, toxicity, hepatic failure, prognostication

INTRODUCTION

Paracetamol is the most widely used over-the-counter medication worldwide, and remains the most common agent involved in overdose cases in Australia and New Zealand (ANZ)(1). This leads to thousands of hospital admissions every year. Most patients with paracetamol poisoning are able to recover after receiving N-

acetylcysteine (NAC or acetylcysteine) and supportive care, however a small proportion develop acute liver failure which is associated with severe adverse outcomes and mortality(2, 3).

Orthotopic liver transplantation (OLT) may be useful in altering survival outcome in acute liver failure (ALF) patients, however the decision to transplant a patient involves a series of complex evaluations, including balancing the risks of delaying OLT against the potential to recover with medical treatment alone, the risks of surgery and psychosocial implications which deem an individual unsuitable for OLT despite fulfilling the transplant criteria(4). Consequently, accurate prognostication is key in managing paracetamol overdose ALF cases to stratify between those who need medical management as opposed to those that may require a liver transplant in order to optimise outcome.

While there are various criteria to predict patients who might benefit from a liver transplant, the King's College Criteria (KCC) for paracetamol toxicity remains one of the most widely used around the world(4) and referral criteria to a liver unit in the UK are based on these.

The ANZ criteria for referral to a liver transplant unit in the setting of paracetamol overdose follows broader criteria that incorporates several different parameters, including lactate, blood pressure, glucose level and the degree of thrombocytopenia (1). Clinicians in the emergency department and hospital system use these criteria to refer patients to a liver unit, but this does not necessarily dictate whether a patient receives a transplant. The ANZ criteria has not been previously analysed for its predictive purpose.

The aim of this study was to analyse the ANZ liver referral criteria to a liver transplant unit post paracetamol overdose for predicting outcome in the setting of ALF.

- **METHODS**

This is a retrospective cohort study of all patients who were admitted with paracetamol toxicity via the Austin Emergency Department and the Liver Transplant Unit from January 2010 to the end of March 2019 (Figure 1). It is a review of data extracted from the electronic record (PowerChart™, V 2012.01, 2013, CERNER, USA) and Medtrack (2015.1, 2014, AUSTRALIA).

Patient Selection

Patients who were admitted between 1 January 2010 and end of March 2019 were screened using ICD codes (Y39.1, X60, X40 and Y10) to identify those who had paracetamol overdose or intoxication. We identified all paracetamol overdose patients and included those who received acetylcysteine. We included patients who developed hepatotoxicity (defined as alanine transaminase (ALT) >1000 U/L). Patients with ambiguity regarding the aetiology of the hepatic dysfunction were

excluded. Patients either had a documented toxic serum paracetamol concentration or a non-detectable paracetamol concentration in the context of a history of paracetamol ingestion reported with a time course consistent with hepatic dysfunction. Patients without a clear history of paracetamol ingestion, including those with an overdose of an unknown agent were excluded. Patients who did not receive acetylcysteine were excluded. Amongst those who received acetylcysteine, each record was manually reviewed to ensure eligibility and confirm the reason for acetylcysteine. If an individual had multiple admissions during the study period, each episode was treated as a different presentation.

The primary endpoint was mortality or transplant, assessed using the ANZ criteria for liver transplant referral.

The KCC is used to help determine need for transplant for patients with paracetamol overdose in this hospital. In addition, we examined the KCC in the same cohort.

Definitions

The ANZ referral criteria and KCC are listed in Figure 2. Hypoglycaemia is defined as a venous or arterial glucose level of ≤ 3.9 mmol/L per international definitions (5). Severe thrombocytopenia is defined as a platelet level of $< 50 \times 10^9$ per litre of blood (6). Any alteration of consciousness is defined as a GCS < 15 not associated with sedative co-ingestions. Determination of grade III/IV encephalopathy was based off clinical documentation in patients' clinical notes. Acute liver injury (ALI) was defined as ALT > 150 U/L and double baseline.

Data extraction

Data extracted from the medical records included age, sex, weight, reason for the ingestion, staggered or once-off ingestion, co-ingestants, initial and post treatment paracetamol concentration (number of hours after ingestion that the serum concentration was obtained), acetylcysteine dosage and duration. Along with co-morbidities such as alcohol abuse, pre-existing renal failure, diabetes and psychiatric conditions. Laboratory parameters recorded included initial and peak ALT, peak Aspartate Aminotransferase (AST) and International Normalised Ratio (INR) and peak creatinine. Prothrombin time (PT), glucose level, blood pressure, serum pH, platelet levels, the need for transplant, length of stay and disposition was also recorded.

The data was collected using a standardised extraction form and entered into a spreadsheet Excel 2019 (version 16.22) by investigators. The 2 abstractors were not blinded to the original study hypothesis.

Ethics approval for the study was obtained from the Austin Health ethics committee.

Data analysis

Descriptive data are reported as medians and interquartile range (IQR) or percentages. The Chi square test was used to compare nominal variables or the Mann-Whitney U test for non-parametric continuous variables. Data analysis was performed using SPSS version (V26, IBM, New York, USA).

Sensitivity, specificity, PPV, NPV were calculated for the ANZ criteria prior to transfer to the liver transplant unit (ie. at time of referral). This same analysis was also performed on these patients to determine if they met the KCC during hospital admission.

RESULTS

A total of 983 presentations with a diagnosis of paracetamol overdose were identified during the period of 2010 to end of March 2019. Of these, 81 (8%) developed hepatotoxicity and were treated with acetylcysteine in the hospital (Figure 1). Sixteen (20% of those who developed hepatotoxicity) patients reached the primary endpoint of death. All of these were deemed secondary to paracetamol overdose. Of those who developed hepatotoxicity, 17 (21%) cases reached the primary endpoint of death or transplant secondary to paracetamol overdose.

Demographic data of this study population is shown in Table 1. The majority of presentations were female with a deliberate intent to overdose in both groups. There was no significant difference in the median (IQR) age between the survivor group and those who died ($p=0.2$). The median time from ingestion to acetylcysteine treatment also varied amongst the two cohorts, with the mortality group being treated much later at 33 hours (IQR 25, 92) compared to the survival group at 24 hours (13, 40) ($p<0.01$). The median treatment duration of acetylcysteine was longer in the mortality group at 62 hours (IQR 34, 157) versus 36 hours (6,85) in the survival group ($P=0.01$).

The sensitivity and specificity of the KCC and ANZ referral criteria to predict mortality or transplant is shown in Table 2. The ANZ referral criteria is highly sensitive at predicting the primary endpoint of death or transplant at time of referral 100% (95%CI: 81, 100) but had poor specificity at 30% (95%CI: 19, 42). KCC criteria applied during hospital admission demonstrated a high sensitivity and specificity for predicting mortality or transplant (sensitivity 94% (71, 100), specificity 91% (81, 97). However the positive predictive value of the KCC was 73% (55, 85).

Arterial acidosis and creatinine were the most common components in the KCC criteria met by the survival group at 7.8% ($n=5$) for each. Persistent acidosis or arterial lactate >3 was the most common component in the ANZ criteria met by the survival group at 57.8% ($n=37$) (Table 3). In the mortality group, arterial acidosis was the most commonly met KCC criteria at 78% ($n=13$), and similarly persistent acidosis or arterial lactate >3 with the ANZ criteria 100% ($n=17$).

DISCUSSION

For patients with severe paracetamol-induced liver toxicity, liver transplant must be considered in those with acute liver failure (7). The decision to transplant a patient requires evaluating carefully the risks of delaying transplant against the potential to recover with medical treatment alone, in addition to risks of surgery and psychosocial implications that deem an individual unsuitable for transplant despite

fulfilling the transplant criteria. The accurate prognostication of outcome in the management of paracetamol induced acute liver failure is crucial in order to stratify individuals who may benefit from a liver transplant, identifying them early before deterioration. Also it may prevent unnecessary transfer to a transplant centre for those who do not require a transplant.

The ANZ referral criteria had a high sensitivity in regards to predicting mortality or transplant and fits its purpose to be a broad screening criteria. This is important in identifying patients who may later deteriorate and become too unstable and difficult to transfer or subsequently receive a liver transplant. Also it allows early discussion with the liver unit on management e.g. use of blood products. In addition, the high negative predictive value indicates that patients have a low risk of mortality if none of the criteria are met at time of referral. However, the ANZ referral criteria revealed a lower specificity and predictive ability for the primary outcome compared to the KCC. This is understandable given the ANZ referral criteria was not designed for the purpose of predicting mortality. Treating clinicians are therefore reminded that discussions with the liver transplant unit needs to occur on who is transferred for paracetamol overdose.

Our study found that the KCC has high overall specificity and sensitivity. This result aligns with multiple studies that have evaluated the KCC in the past in paracetamol induced ALF populations to reveal a high pooled specificity at 94.6% (95% CI 93.0, 95.9) but is contrary to the relatively poor sensitivity at 58.2% (95% CI 53.1, 63.3) seen previously (4). The high specificity of the KCC during admission is understandable because patients usually have progressed further within their course of paracetamol induced acute liver failure, therefore rendering it a more accurate predictor of mortality or transplant. However, the lower positive predictive value indicates that not all patients who fulfill the KCC criteria will die or require a transplant.

In addition, a recent study indicated a high rate of transplant free survival in contemporary and historical cohorts (73.8% (Year 2002 to 2017) vs 69% (Year 1988-2001), $p=0.614$) of those with paracetamol overdose. This probably highlights the importance of supportive care and the advantages of early recognition of acute liver failure and referral to a specialised liver unit(8).

Hypotension in ALF is well recognised, as cardiovascular and haemodynamic complications are notable clinical sequelae of ALF patients often characterised by systemic vasodilation, low systemic vascular resistance, hypotension and a compensatory increase in cardiac output(9). Hypotension has also been incorporated in other assessment criteria such as the sequential organ failure assessment (SOFA) score to assess the prognosis of patients with ALF. In addition to this, it was also found that the prolongation of PT that reflects the severity of liver damage is significantly longer in patients with unexplained hypotension(10). The results of our study support that hypotension could be an important prognostic factor needing further evaluation in the future.

Grade III encephalopathy is characterised by marked confusion and incoherent speech, grade IV patients further deteriorates to a coma state and become unresponsive to pain(11). Hepatic encephalopathy usually develops 3 to 4 days after paracetamol overdose, and it is accompanied with an increased risk of overall death rate at 40-60% once it emerges(12). Studies have shown that transplant-free survival further dropped from 52% to 33% when coma grade increases from grade I/II encephalopathy to grade III/IV(13). Although high grade encephalopathy is evaluated to be a good predictor of overall mortality (12, 13), it is limited by its subjective nature and the time delay for patients to progress to this stage. Up to 26% of paracetamol overdose patients are no longer medically fit for surgery when they fulfil the KCC(14). At this point, their treatment has been delayed and they are also unable to participate in further psychosocial evaluations(13). Therefore, although high grade encephalopathy carries high predictive value, it is vital to seek out alternative criteria to increase its sensitivity earlier in the natural history of ALF. It is crucial that prognostic criteria allow patients to be picked up early prior to the development of high-grade encephalopathy in order for them to undergo necessary assessments and planning for a liver transplant.

Persistent acidosis and acute renal failure were both present in a majority of patients who died from paracetamol overdose in our study. These findings correlate with other studies that have shown that a $\text{pH} < 7.30$ carries high predictive accuracy for death(15-17). In addition, elevated serum creatinine has also been identified in regression models from other studies to be a good indicator for a poor prognosis in paracetamol induced liver failure (15).

Limitations

The study is limited by its retrospective design. As a result, the conclusions are limited by the quality and completeness of the data recorded in the medical record. In addition, the small number of patients with mortality limited further regression modelling. Medical and supportive care for patients has likely improved over time which may have also decreased mortality rates and need for transplant. Another limitation was that there was no data on patients who met either criteria who were not transferred or who died prior to transfer. The results of this study provide the framework for the design of larger future multicentre studies to further evaluate these referral models.

CONCLUSION

The ANZ referral criteria was highly sensitive for predicting the outcome of mortality and transplant. This is important for screening patients that may become unstable and difficult to transfer at a later stage of their admission.

Data availability statement: The data are not publicly available due to privacy or ethical restrictions.

REFERENCES

1. Chiew AL, Reith D, Pomerleau A, Wong A, Isoardi KZ, Soderstrom J, et al. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. *The Medical journal of Australia*. 2020;212(4):175-83.
2. Doyon S, Klein-Schwartz W. Hepatotoxicity Despite Early Administration of Intravenous N-Acetylcysteine for Acute Acetaminophen Overdose. *Academic Emergency Medicine*. 2009;16(1):34-9.
3. Lee WM. Acute liver failure. *Seminars in respiratory and critical care medicine*. 2012;33(1):36-45.
4. Craig DG, Ford AC, Hayes PC, Simpson KJ. Systematic review: prognostic tests of paracetamol-induced acute liver failure. *Alimentary pharmacology & therapeutics*. 2010;31(10):1064-76.
5. Chiew AL, Fountain JS, Graudins A, Isbister GK, Reith D, Buckley NA. Summary statement: new guidelines for the management of paracetamol poisoning in Australia and New Zealand. *The Medical journal of Australia*. 2015;203(5):215-8.
6. Williamson DR, Albert M, Heels-Ansdell D, Arnold DM, Lauzier F, Zarychanski R, et al. Thrombocytopenia in critically ill patients receiving thromboprophylaxis: frequency, risk factors, and outcomes. *Chest*. 2013;144(4):1207-15.
7. Ding GK, Buckley NA. Evidence and consequences of spectrum bias in studies of criteria for liver transplant in paracetamol hepatotoxicity. *QJM : monthly journal of the Association of Physicians*. 2008;101(9):723-9.
8. Hey P, Hanrahan TP, Sinclair M, Testro AG, Angus PW, Peterson A, et al. Epidemiology and outcomes of acute liver failure in Australia. *World J Hepatol*. 2019;11(7):586-95.
9. Bernal W, Lee WM, Wendon J, Larsen FS, Williams R. Acute liver failure: A curable disease by 2024? *Journal of hepatology*. 2015;62(1, Supplement):S112-S20.
10. Trewby PN, Williams R. Pathophysiology of hypotension in patients with fulminant hepatic failure. *Gut*. 1977;18(12):1021-6.
11. Dharel N, Bajaj JS. Definition and Nomenclature of Hepatic Encephalopathy. *Journal of Clinical and Experimental Hepatology*. 2015;5:S37-S41.
12. Schiodt FV, Bondesen S, Tygstrup N, Christensen E. Prediction of hepatic encephalopathy in paracetamol overdose: a prospective and validated study. *Scandinavian journal of gastroenterology*. 1999;34(7):723-8.
13. Renner EL. How to decide when to list a patient with acute liver failure for liver transplantation? Clichy or King's College criteria, or something else? *Journal of hepatology*. 2007;46(4):554-7.
14. Simpson KJ, Bates CM, Henderson NC, Wigmore SJ, Garden OJ, Lee A, et al. The utilization of liver transplantation in the management of acute liver failure: comparison between acetaminophen and non-acetaminophen etiologies. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society*. 2009;15(6):600-9.
15. Anand AC, Nightingale P, Neuberger JM. Early indicators of prognosis in fulminant hepatic failure: an assessment of the King's criteria. *Journal of hepatology*. 1997;26(1):62-8.
16. Izumi S, Langley PG, Wendon J, Ellis AJ, Pernambuco R, Hughes RD, et al. Coagulation factor V levels as a prognostic indicator in fulminant hepatic failure. *Hepatology (Baltimore, Md)*. 1996;23(6):1507-11.

17. O'Grady JG, Alexander GJ, Hayllar KM, Williams R. Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology*. 1989;97(2):439-45.

Figure 1: Study Flowchart

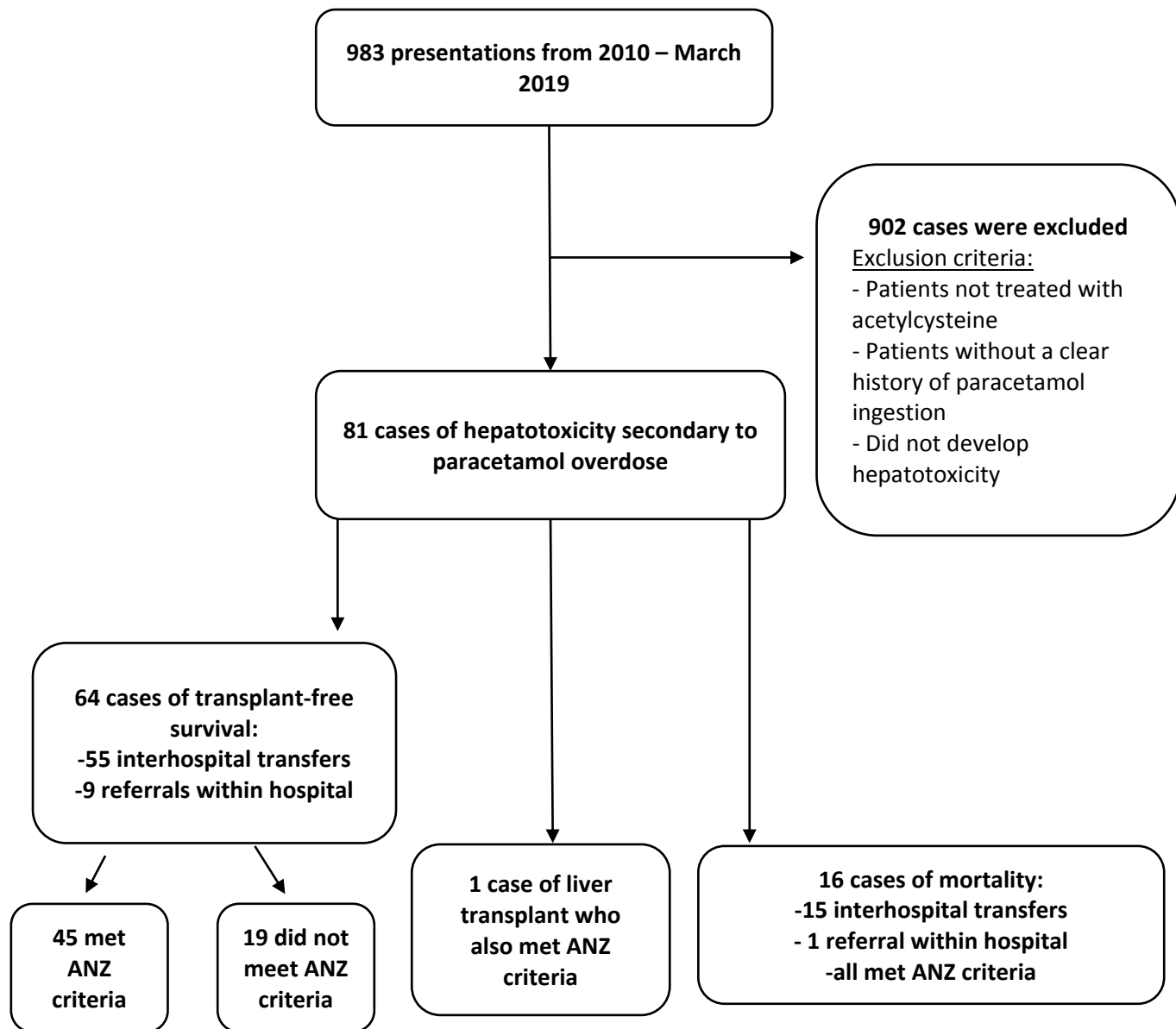


Figure 2: King’s College Criteria and Australia and New Zealand referral criteria.

King's College Criteria for consideration liver transplant	ANZ criteria for transfer to a liver transplant unit
<ul style="list-style-type: none"> • Arterial pH < 7.30 OR all 3 of the following: • PT > 100 sec • Creatinine > 300 µmol/L • Grade III or IV hepatic encephalopathy 	<ul style="list-style-type: none"> • INR > 3.0 at 48 hours or > 4.5 at any time • Oliguria or creatinine > 200 µmol/L • Persistent acidosis (pH <7.3) or arterial lactate > 3mmol/L, despite resuscitation • Systolic hypotension with BP <80 mmHg, despite resuscitation • Hypoglycaemia • Severe thrombocytopenia • Encephalopathy of any degree • Any alteration consciousness (GCS<15), not associated with sedative co-ingestions

Table 1. Demographic and treatment data of patients presenting with paracetamol overdose treated with acetylcysteine who developed hepatotoxicity (ALT >1000

U/L). ALT=alanine transaminase, AST-aspartate transaminase, INR –international normalized ratio

	<i>Survived (n=64)</i>	<i>Death/transplant (n=17)</i>	<i>P value</i>
Gender female n (%)	55 (86)	15 (88)	0.8
Median Age years (IQR)	36 (23,48)	40 (34,46)	0.2
Intent - deliberate n (%)	40 (63)	14 (78)	0.12
- Single ingestion n	22 (34)	0	<0.01
- Supratherapeutic n (%)	14 (22)	3 (17)	0.7
- Staggered intake n (%)	4 (6)	11 (61)	<0.001
Time to acetylcysteine ($\leq 8h$) n (%)	0	0	
Median length of stay – hours (IQR)	204 (96,474)	84 (48, 366)	0.03
Disposition – home n (%)	56 (88)	0	<0.001
- Psych admission n (%)	8 (12)	0	<0.001
Transplant n (%)	0	1 (5)	<0.001
Death n (%)	0	16 (94)	<0.001
Coingestion n (%)	28 (44)	10 (59)	0.26
- Opioids n (%)	4 (6)	1 (6)	0.95
- Antihistamines n (%)	3 (4)	0 (0)	<0.001
- ETOH n (%)	9 (14)	7 (41)	0.01
Activate Charcoal administration n (%)	0	1 (6)	<0.001
Chronic alcohol intake n (%)	15 (23)	7 (41)	0.14
Median reported paracetamol dose for ingestions by weight mg/kg	385 (230,625)	250 (166,390)	<0.001
Median serum paracetamol concentration micromol/L on presentation (IQR)	300 (89,635)	507 (149, 969)	0.23
Median time to initial paracetamol concentration – hours (IQR)	23 (12,35)	33 (24, 88)	<0.001
Median acetylcysteine duration hours (IQR)	36 (6,85)	62 (34, 157)	0.01
Median ALT (U/L) on arrival (IQR)	1011 (229,4769)	2635 (869, 8779)	0.01
Median peak ALT (IQR)	6751 (3113,9394)	7121 (4688, 10480)	0.18
Median peak AST (U/L) (IQR)	7973 (5054,13212)	13420 (4692, 18684)	0.04
Median Peak INR (IQR)	4.3 (2.2,6.4)	6.8 (5.5,7.8)	0.003

Median Peak Cr $\mu\text{mol/L}$ (IQR)	101 (71,271)	179 (140, 321)	<0.001
--	--------------	----------------	--------

*IQR: Interquartile range

Table 2. Sensitivity and Specificity of the King's College Criteria (KCC) and Australian and New Zealand (ANZ) referral criteria to predict death/transplant

Hepatotoxicity patients (ALT >1000)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	PPV (95% CI)	NPV (95% CI)
KCC during admission	94% (71, 100)	90% (80, 97)	10.0 (5, 22)	0.06 (0.01, 0.4)	73% (55, 85)	98% (89, 100)
ANZ on referral to liver transplant unit	100% (81, 100)	30% (19, 42)	1.5 (1.2, 1.7)	0	27% (24, 31)	1

Table 3. % of survival and mortality group that met each component in the i) KCC and ii) ANZ criteria.

i)

KCC Criteria component	% of survival group meeting criteria (n)	% of mortality group meeting criteria (n)
<i>Arterial PH <7.3</i>	7.8% (5)	77.8% (13)
<i>PT >100</i>	3.1% (2)	5.9% (1)
<i>Cr >300</i>	7.8% (5)	11.7% (2)
<i>Grade III/IV encephalopathy</i>	6.3% (4)	58.8% (10)

ii)

ANZ Criteria component	% of survival group meeting criteria (n)	% of mortality group meeting criteria (n)
<i>INR >3 at 48 hours or >4.5 at any time</i>	54.7% (35)	88.2% (15)
<i>Oliguria or Cr >200</i>	40.6% (26)	76.4% (13)
<i>Persistent acidosis or Arterial Lactate >3 despite resuscitation</i>	57.8% (37)	100% (17)
<i>Systolic hypotension (BP <80mmHg)</i>	0	35.3% (6)
<i>Hypoglycaemia</i>	1.6% (1)	11.8% (2)
<i>Severe thrombocytopenia</i>	1.6% (1)	11.8% (2)
<i>Encephalopathy of any degree</i>	29.7% (19)	88.2% (15)
<i>Any alteration consciousness (GCS <15), not associated with sedative co-ingestions</i>	29.7% (19)	88.2% (15)

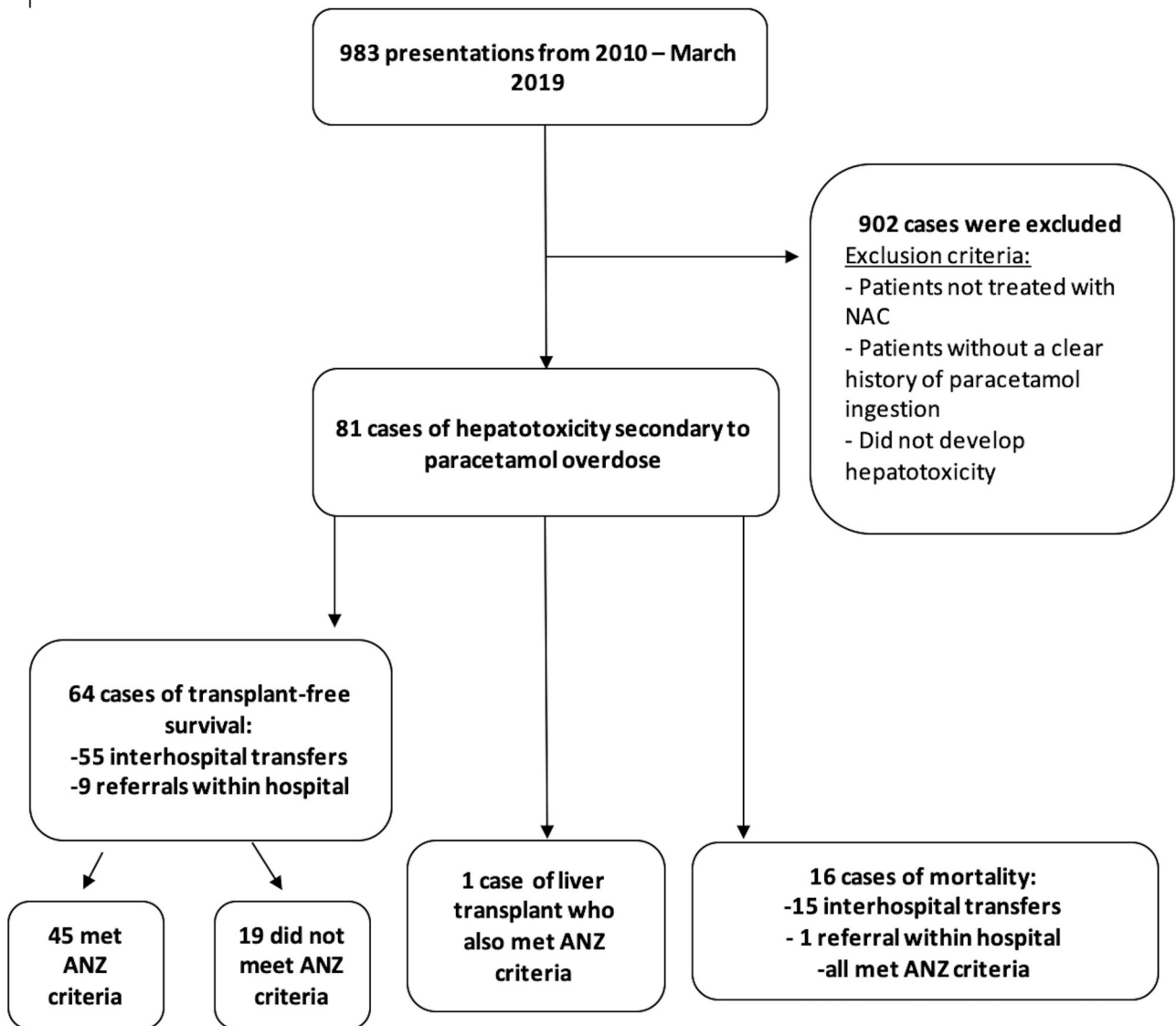
Appendix 1: King's College Criteria (KCC) met during hospital admission and Australia and New Zealand (ANZ) criteria performed at time of referral.

KCC

KCC	Mortality	No mortality
Criteria met	16	6
Criteria not met	1	58

ANZ

ANZ	Mortality	No mortality
Criteria met	17	45
Criteria not met	0	19



EMM_13795_Figure 1.jpg

King's College Criteria for consideration liver transplant	ANZ criteria for transfer to a liver transplant unit
<ul style="list-style-type: none"> • Arterial pH < 7.30 OR all 3 of the following: • PT > 100 sec • Creatinine > 300 µmol/L • Grade III or IV hepatic encephalopathy 	<ul style="list-style-type: none"> • INR > 3.0 at 48 hours or > 4.5 at any time • Oliguria or creatinine > 200 µmol/L • Persistent acidosis (pH <7.3) or arterial lactate > 3mmol/L, despite resuscitation • Systolic hypotension with BP <80 mmHg, despite resuscitation • Hypoglycaemia • Severe thrombocytopenia • Encephalopathy of any degree • Any alteration consciousness (GCS<15), not associated with sedative co-ingestions

EMM_13795_Figure 2.jpg