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Development and Validation of a Renal Replacement after Trauma Scoring Tool

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Brief Title: Renal Replacement after Trauma Scoring Tool

Background: Stress on the healthcare system requires careful allocation of resources such as renal replacement therapy (RRT). The COVID-19 pandemic generated difficulty securing access to RRT for trauma patients. We sought to develop a renal replacement after trauma (RAT) scoring tool to help identify trauma patients who may require RRT during their hospitalization.

Study Design: The 2017-2020 Trauma Quality Improvement Program (TQIP) database was divided into a derivation (2017-2018 data) and validation (2019-2020 data) set. A three-step methodology was used. Adult trauma patients admitted from the emergency department (ED) to the operating room or intensive care unit were included. Patients with chronic kidney disease, transfers from another hospital, and ED deaths were excluded. Multiple logistic regression models were created to determine the risk for RRT in trauma patients. The weighted average and relative impact of each independent predictor was used to derive a RAT score, which was validated using area under receiver-operating characteristic curve (AUROC).

RESULTS: From 398,873 patients in the derivation and 409,037 patients in the validation set, 11 independent predictors of RRT were included in the RAT score derived with scores ranging from 0-11. The AUROC for the derivation set was 0.85. The rate of RRT increased to 1.1%, 3.3%, and 20% at scores of 6, 8, and 10, respectively. The validation set AUROC was 0.83.

CONCLUSION: RAT is a novel and validated scoring tool to help predict the need for RRT in trauma patients. With future improvements including baseline renal function and other variables, the RAT tool may help prepare for the allocation of RRT machines/staff during times of limited resources.

Keywords: renal replacement therapy, dialysis, trauma, kidney failure, scoring tool, TQIP

Abbreviations:

RRT - renal replacement therapy

RAT - renal replacement after trauma

AUROC - area under receiver-operating characteristic curve

OR: odds ratio

Introduction

Renal replacement therapy (RRT) is a life-saving treatment for patients with insufficient renal function. This includes over 618 million people worldwide and more than 560,000 people in the United States who are currently on dialysis, with its incidence continuing to increase.[1-3] Despite its critical importance, resources for RRT have been severely limited and this shortage was exacerbated by the unprecedented needs of the recent COVID-19 pandemic.[1,2] Trauma patients are at particularly high-risk for suffering acute kidney injury, with rates as high as 67% amongst the most severely injured.[3] While the historical incidence for the need of post-traumatic RRT is <1%, there is evidence that timely initiation of RRT improves mortality in trauma patients.[4–7] Furthermore, the ability to identify trauma patients early who eventually require RRT would allow providers and hospital administrators the opportunity to triage resources to provide optimal care.

Currently, there are several prediction models to evaluate patients with chronic kidney disease who will progress to need RRT.[8–14] However, no tool has been developed to predict the need for RRT in trauma patients. The purpose of this study is to develop and validate a novel Renal replacement After Trauma (RAT) scoring tool to help identify trauma patients who require RRT during their index hospitalization. An accurate and validated scoring tool could serve to identify high-risk patients allowing appropriate counseling and ensuring the availability of RRT, especially in a time of resource limitation.

Methods

This study was conducted through a retrospective review of the Trauma Quality Improvement Program (TQIP) database, a multicenter database that systematically collects

prospective trauma data by trained professionals. This study was deemed exempt by our institutional review board, and a waiver of informed consent granted.

The RAT scoring tool was created using a 3-step method, described previously.[15–17] The 2017-2018 TQIP dataset was queried for trauma patients who were 18 years of age or older and admitted from the emergency department (ED) to the operating room (OR) or intensive care unit (ICU). Also, any trauma patient admitted initially to the surgical floor but subsequently was upgraded to the ICU during their hospitalization was included, as these patients may potentially require RRT. Patients with chronic kidney disease, transferred from another hospital, or who died in the ED were excluded. This 2017-2018 data served as the derivation set to develop the RAT scoring tool. The dataset was separated into two groups. All trauma patients who required RRT (either hemodialysis or continuous RRT) during the index hospitalization were included in the (+) RRT group. All others comprised the (-) RRT group. A univariate analysis was used to compare the two groups based on demographics (e.g., age and sex) and comorbidities (e.g., cirrhosis, diabetes, hypertension, and congestive heart failure). In addition, injury profile data including specific organ injuries were recorded. Finally, operations (based on International Classification of Diseases codes) and complications including packed red blood cell transfusions, sepsis, unplanned intubation, ICU admission or return to the OR, ventilator days, length of stay and mortality were collected. Variables with a p-value < 0.2 were included in stepwise multivariate logistic regression models to identify independent risk factors for RRT. Additional variables associated with acute kidney injury and failure such as hypotension on arrival, rhabdomyolysis, obesity, and performance of a fasciotomy were considered for inclusion in the scoring model based on author consensus and a review of existing literature.[18–21] The weighted average and odds ratio of each independent factor were used to inform multiple iterations of the

scoring tool, which was simplified to provide its ease of use. The area under the receiver-operating curve (AUROC) was calculated after each iteration to verify its continued accuracy.

After deriving the RAT scoring tool, validation was performed using the 2019-2020 TQIP dataset, using the same inclusion/exclusion criteria. An AUROC was performed based on the 2019-2020 dataset and directly compared to the AUROC of the derivation 2017-2018 dataset for validation of the RAT Scoring Tool. All analyses were performed with IBM SPSS Statistics for Windows (version 24, IBM Corp, Armonk, NY).

Results

Of 398,873 trauma patients included in the 2017-2018 TQIP derivation dataset, 665 (0.17%) required RRT with 224 (33.7%) of those requiring continuous RRT and 476 (71.6%) requiring intermittent RRT. When comparing the (+) RRT group with the (-) RRT group, the (+) RRT group was older (57 vs. 50-years-old, $p<0.001$) and more commonly male (75.3% vs. 68.4%, $p<0.001$). Compared to the (-) RRT group, the (+) RRT group had increased rates of multiple comorbidities and functional impairment, however, a decreased rate of dementia **(Table 1)**.

Regarding injuries, the (+) RRT cohort had higher rates of spine fractures (36.2% vs. 21.8%, $p<0.001$), spinal cord injuries (5.1% vs. 3.6%, $p=0.034$), cardiac injuries (3.6% vs. 0.9%, $p<0.001$), rib fracture (44.7% vs. 24.7%, $p<0.001$), pneumothorax (17.4 vs. 10.8%, $p<0.001$), lung injury (40.2% vs. 21.5%, $p<0.001$), pelvic fracture (24.4% vs. 8.7%, $p<0.001$) and lower extremity fracture (36.2% vs. 24.5%, $p<0.001$). The (+) RRT also had higher rates of surgery on the respiratory (43.8% vs. 8.8%, $p<0.001$), gastrointestinal (45.9% vs. 12.8%, $p<0.001$), hepatobiliary (14.3% vs. 1.7%, $p<0.001$), and urinary (40.8% vs. 16.2%, $p<0.001$) systems including nephrectomy (2.0% vs. 0.2%, $p<0.001$) **(Table 2)**.

The (+) RRT group had higher rates of hypotension on arrival (19.3% vs. 6.0%, p<0.001), packed red blood cell transfusion within 4 hours of presentation (35.9 vs. 9.8%, p<0.001). The (+) RRT group also suffered higher rates of in-hospital complications such as extremity compartment syndrome (2.3% vs. 0.2%, p<0.001), rhabdomyolysis (0.3% vs. 0%, p<0.001), fasciotomy (2.0% vs. 0.3%, p<0.001), sepsis (15.8% vs. 0.7%, p<0.001), unplanned intubation (17.3% vs. 2.5%, p<0.001), unplanned ICU admission (15.8% vs. 3.8%, p<0.001), unplanned return to OR (10.7% vs. 1.2%, p<0.001), and mortality (35.3% vs. 7.5%, p<0.001) **(Table 3)**. Additionally, the (+) RRT group had increased ventilator days (12 days vs. 3 days, p<0.001), ICU length of stay (14 days vs. 3 days, p<0.001), and hospital length of stay (22 days vs. 6 days, p<0.001) **(Table 4)**.

Multiple logistic regression models identified 11 independent predictors of RRT which were male sex, mechanical ventilation, comorbidities such as cirrhosis, diabetes, hypertension or congestive heart failure, hypotension on arrival, packed red blood cell transfusion within 4 hours of presentation, operation involving the respiratory, gastrointestinal, hepatobiliary, and urinary system within 24 hours of presentation, renal injury, and lower extremity fracture. Each predictor had a similar effect on the risk for RRT and the RAT score was derived with scores ranging from 0-11 with each variable carrying equal weight **(Table 5)**. The AUROC for the derivation set was 0.85. The rate of RRT increased steadily from 1.1%, 3.3%, and 20% at scores of 6, 8, and 10, respectively **(Figure 1)**. Few patients achieved a RAT score of 11 and therefore the incidence of RRT could not be calculated for the maximum RAT score.

The TQIP 2019-2020 validation dataset was comprised of 409,037 patients who met inclusion/exclusion criteria for the RAT Scoring Tool validation analysis. The AUROC curve for the validation set was 0.83, similar to the derivation set **(Figure 2)**.

Discussion

RRT is an expensive and labor-intensive, albeit life-saving resource.[22] In order to maximize the benefit from such a limited resource, it is prudent for health care providers and administrators to identify potential patients who will require RRT at an early stage in their hospitalization. While there are tools utilized to predict RRT need for patients with chronic kidney disease, no such tool has been developed for trauma patients, which represents an increasing population nationally as the general population ages.[8–14,23,24] This large national analysis spanning 4 years of data identified risk factors for RRT in adult trauma patients who are most susceptible to develop acute renal failure after injury (i.e., admission to the OR from ED or admission to the ICU at some point during their hospitalization). These risk factors include male sex, mechanical ventilation, comorbidities (i.e., cirrhosis, diabetes, hypertension, or congestive heart failure), hypotension on arrival, packed red blood cell transfusion within 4 hours of presentation, operation involving the respiratory, gastrointestinal, hepatobiliary, and urinary system within 24 hours of presentation, renal injury, and lower extremity fracture. As a result, an easy-to-use integer-based RAT scoring tool was developed and validated using contemporary nationwide data from trauma patients.

Most of the risk factors identified in this study are known to have an impact on renal failure following injury which provides further justification for their inclusion in the novel RAT scoring tool.[4,6,18,25] In addition, a major advantage of the RAT scoring tool is its simplicity and the availability of most variables shortly after presentation which allows for a timely identification of trauma patients who may need RRT. The only variables not immediately available could be the transfusion within 4 hours and select operations within 24 hours, however

both of these variables are known within 24-hours of presentation and thus still occur early enough in hospitalization to aid with prognostication and resource allocation.

There are other variables such as rhabdomyolysis and obesity, that have been demonstrated in prior studies to predict renal failure in trauma patients.[19–21] These variables were also more common in patients receiving RRT in this study. However, the addition of rhabdomyolysis and obesity lowered the quality of the RAT scoring tool and thus were excluded from the RAT score. Also, having all variables readily available provided further support for excluding rhabdomyolysis from the RAT scoring tool as well. Additionally, sickle-cell disease/trait has been shown to be a risk factor for exertional rhabdomyolysis but its association with post-traumatic RRT could not be evaluated as no patients within the RRT group carried the diagnosis.[26] Lastly, fasciotomy was evaluated for inclusion in the RAT Scoring Tool but did not improve the model and was excluded to maintain ease-of-use. Future studies are needed to evaluate these findings and determine if a more narrow subset of these variables may prove helpful in further honing the RAT scoring tool.

This study has numerous limitations, including the inherent potential for misclassification and missing variables within a large national dataset. There are also institutional variations in criteria for initiation of RRT which are not accounted for in this analysis as this data is not available within TQIP. Additionally, TQIP does not provide information regarding the time to initiation of RRT and the use of intravenous contrast for imaging so its effects on renal failure cannot be evaluated. Although, recent studies have shown intravenous contrast does not affect renal complications.[27,28] In terms of methodology, there are multiple techniques to develop risk scoring tools such as machine learning or decision tree analysis that may prove more helpful. However our technique for the development of the RAT tool has been utilized in prior studies[15–

[17] and decision tree analysis favors the most common variables rather than focusing on the most predictive variables. As these most predictive variables for RRT are not the most common, decision tree analysis may not prove as helpful as our current methodology, but merits future study.

Also, there are several other known predictors of acute renal failure including, but not limited to, urine output, baseline serum creatinine, creatine phosphokinase, intravenous fluid balance, serum lactate, mean arterial pressure, hemorrhagic shock duration, and exposure to nephrotoxic medications which are not available within TQIP.[6,19,21,25,29] Acknowledging this, we believe this current study serves as a scaffold for future prospective studies to build upon and incorporate more granular data (i.e., serum lactate/creatinine, urine output, and continuous physiologic data) to further hone the RAT Scoring Tool. Finally, it is important to acknowledge the limitations of clinical application for the RAT score in its current form given that the highest predicted risk of post-traumatic RRT is 20% with a RAT score of 10. Although this predicted risk of 20% is somewhat low, this is over 400 times the national incidence for trauma patients. Furthermore, the RAT Scoring Tool is the first trauma specific risk tool to predict the need for RRT with good predictive capability and has the potential to be an invaluable tool for resource allocation with further improvements.

Conclusion

The RAT score is a novel and validated scoring tool to predict the need for RRT in trauma patients. This tool may be able to help hospital systems better prepare for the allocation of precious resources including RRT machines and trained staff to safely manage patients with acute renal failure, especially during periods when resources are limited. However, prior to

adoption, future prospective studies which incorporate laboratory values and other potential predictors of acute renal failure should be performed to improve its prediction capabilities.

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Figure Legend:

Figure 1: Rate of renal-replacement therapy (RRT) predicted by Renal replacement After Trauma (RAT) Score

Figure 2: Area under the receiver operating characteristic curve (AUROC) for development of the Renal replacement After Trauma (RAT) scoring tool. (**A**) Test set [AUROC=0.85], (**B**) Validation set [AUROC=0.83]

Precis:

This study derives and validates a renal replacement after trauma scoring tool to predict the need for renal replacement therapy in trauma patients.

Table 1. Demographics of Patients Included in The Derivation Dataset Based on Renal Replacement Therapy Requirement

Characteristic	**(-) RRT (n = 398208)**	**(+) RRT (n = 665)**	**p Value**
Age, y, median (IQR)	50 (37)	57 (32)	<0.001
Sex, m, n (%)	272419 (68.4)	501 (75.3)	<0.001
Comorbidity, n (%)			
Cerebral vascular accident	9452 (2.4)	17 (2.6)	0.757
Dementia	13883 (3.5)	11 (1.7)	0.010
ADHD	3898 (1)	5 (0.8)	0.552
Mental health disorder	42589 (10.7)	75 (11.3)	0.627
MI	3223 (0.8)	11 (1.7)	0.015
Congestive heart failure	12822 (3.2)	70 (10.5)	<0.001
Hypertension	119137 (29.9)	305 (45.9)	<0.001
Ventilation	115596 (29)	537 (80.8)	<0.001
COPD	23668 (5.9)	50 (7.5)	0.086
Cirrhosis	4958 (1.2)	43 (6.5)	<0.001
Congenital kidney disease	1245 (0.3)	3 (0.5)	0.523
Diabetes	49473 (12.4)	191 (28.7)	<0.001
Steroids	2916 (0.7)	8 (1.2)	0.155
Peripheral artery disease	2206 (0.6)	11 (1.7)	<0.001
Disseminated cancer	2304 (0.6)	3 (0.5)	0.665
Chemotherapy	1611 (0.4)	2 (0.3)	0.673
Functional impairment	19696 (4.9)	46 (6.9)	0.019
Smoker	88740 (22.3)	120 (18)	0.009
Alcohol use disorder	31858 (8)	58 (8.7)	0.493
Substance abuse	36021 (9)	73 (11)	0.083

ADHD, attention deficit hyperactivity disorder; IQR, interquartile range; RRT, renal-replacement therapy

Table 2. Injuries and Procedures of Patients Included in the Derivation Dataset Based on Renal Replacement Therapy Requirement

Characteristic	(-) RRT (n = 398208)	(+) RRT (n = 665)	p Value
Injury			
Traumatic brain injury	125871 (31.6)	164 (24.7)	<0.001
Skull/facial fracture	84460 (21.2)	108 (16.2)	0.002
Spine fracture	86976 (21.8)	241 (36.2)	<0.001
Cervical spine fracture	33743 (8.5)	64 (9.6)	0.287
Spinal cord	14254 (3.6)	34 (5.1)	0.034
Cervical cord	9540 (2.4)	16 (2.4)	0.986
Thoracic cord	3432 (0.9)	16 (2.4)	<0.001
Thoracic vessel	4364 (1.1)	31 (4.7)	<0.001
Cardiac	3734 (0.9)	24 (3.6)	<0.001
Rib fracture	98288 (24.7)	297 (44.7)	<0.001
Pneumothorax	43027 (10.8)	116 (17.4)	<0.001
Hemothorax	11623 (2.9)	33 (5)	0.002
Hemopneumothorax	18354 (4.6)	90 (13.5)	<0.001
Lung	85621 (21.5)	267 (40.2)	<0.001
Diaphragm	5517 (1.4)	30 (4.5)	<0.001
Esophagus	189 (0)	1 (0.2)	0.224
Stomach	2967 (0.7)	18 (2.7)	<0.001
Small intestine	10701 (2.7)	64 (9.6)	<0.001
Colon	9513 (2.4)	67 (10.1)	<0.001
Rectum	1169 (0.3)	12 (1.8)	<0.001
Kidney	11138 (2.8)	79 (11.9)	<0.001
Ureter	554 (0.1)	5 (0.8)	<0.001
Bladder	2993 (0.8)	25 (3.8)	<0.001
Urethra	907 (0.2)	9 (1.4)	<0.001
Spleen	22297 (5.6)	99 (14.9)	<0.001
Liver	23149 (5.8)	113 (17)	<0.001
Gallbladder	644 (0.2)	5 (0.8)	<0.001
Bile duct	63 (0)	0 (0)	0.746
Pancreas	2735 (0.7)	26 (3.9)	<0.001
Pelvic fracture	34677 (8.7)	162 (24.4)	<0.001
Upper extremity fracture	56965 (14.3)	120 (18)	0.006
Lower extremity fracture	97587 (24.5)	241 (36.2)	<0.001
Injury severity score ≥15	146751 (36.9)	413 (62.1)	<0.001
Operation			
Respiratory	34953 (8.8)	291 (43.8)	<0.001
Gastrointestinal	50950 (12.8)	305 (45.9)	<0.001
Hepatobiliary	6882 (1.7)	95 (14.3)	<0.001
Urinary	64571 (16.2)	271 (40.8)	<0.001
Nephrectomy	770 (0.2)	13 (2.0)	<0.001

Data presented as n (%)

RRT, renal replacement therapy

Table 3. Complications of Patients Included in the Derivation Dataset Based on Renal Replacement Therapy Requirement

Complication	(-) RRT (n = 398208)	(+) RRT (n = 665)	p Value
Cerebrovascular accident	2269 (0.6)	24 (3.6)	<0.001
MI	1302 (0.3)	16 (2.4)	<0.001
Cardiac arrest	7031 (1.8)	117 (17.6)	<0.001
Hypotension on arrival	23498 (6.0)	124 (19.3)	<0.001
Unplanned intubation	9994 (2.5)	115 (17.3)	<0.001
Pulmonary embolism	2830 (0.7)	27 (4.1)	<0.001
Deep vein thrombosis	5613 (1.4)	58 (8.7)	<0.001
PRBC transfusion within 4 hours	38874 (9.8)	239 (35.9)	<0.001
Sepsis	2943 (0.7)	105 (15.8)	<0.001
Ventilator-associated pneumonia	5403 (1.4)	67 (10.1)	<0.001
CAUTI	2042 (0.5)	24 (3.6)	<0.001
CLABSI	447 (0.1)	11 (1.7)	<0.001
Deep SSI	1152 (0.3)	11 (1.7)	<0.001
Extremity compartment syndrome	766 (0.2)	15 (2.3)	<0.001
Rhabdomyolysis	100 (0.0)	2 (0.3)	<0.001
Fasciotomy	998 (0.3)	13 (2.0)	<0.001
Unplanned ICU admission	15059 (3.8)	105 (15.8)	<0.001
Unplanned return to OR	4760 (1.2)	71 (10.7)	<0.001
Mortality	29726 (7.5)	235 (35.3)	<0.001

Data presented as n (%)

CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated blood stream infection; OR, operating room; PRBC, packed red blood cell; RRT, renal replacement therapy; SSI, surgical site infection

Table 4. Outcomes of Patients Included in the Derivation Dataset Based on Renal Replacement Therapy Requirement

Characteristic	**(-) RRT (n = 398208)**	**(+) RRT (n = 665)**	**p Value**
Ventilator days	3 (6)	12 (17)	<0.001
ICU length of stay, d	3 (4)	14 (23)	<0.001
Length of stay, d	6 (8)	22 (29)	<0.001

Data presented as median (interquartile range)
RRT, renal replacement therapy

Table 5. Development of the Renal Replacement After Trauma Scoring Tool

Variable	Points
Sex, m	1
Mechanical ventilation	1
History of cirrhosis, DM, HTN, or CHF	1
Hypotension on arrival	1
PRBC transfusion within first 4 h	1
Respiratory system operation within first 24 h	1
Gastrointestinal system operation within first 24 h	1
Hepatobiliary system operation within first 24 h	1
Urinary system operation within first 24 h	1
Renal injury	1
Lower extremity fracture	1
Maximum score	11
AUROC	0.85
95% CI for AUROC	0.83-86

AUROC, area under receiver-operating characteristic curve; CHF, congestive heart failure; DM, diabetes mellitus; HTN, hypertension; PRBC, packed red blood cell

Figure 1

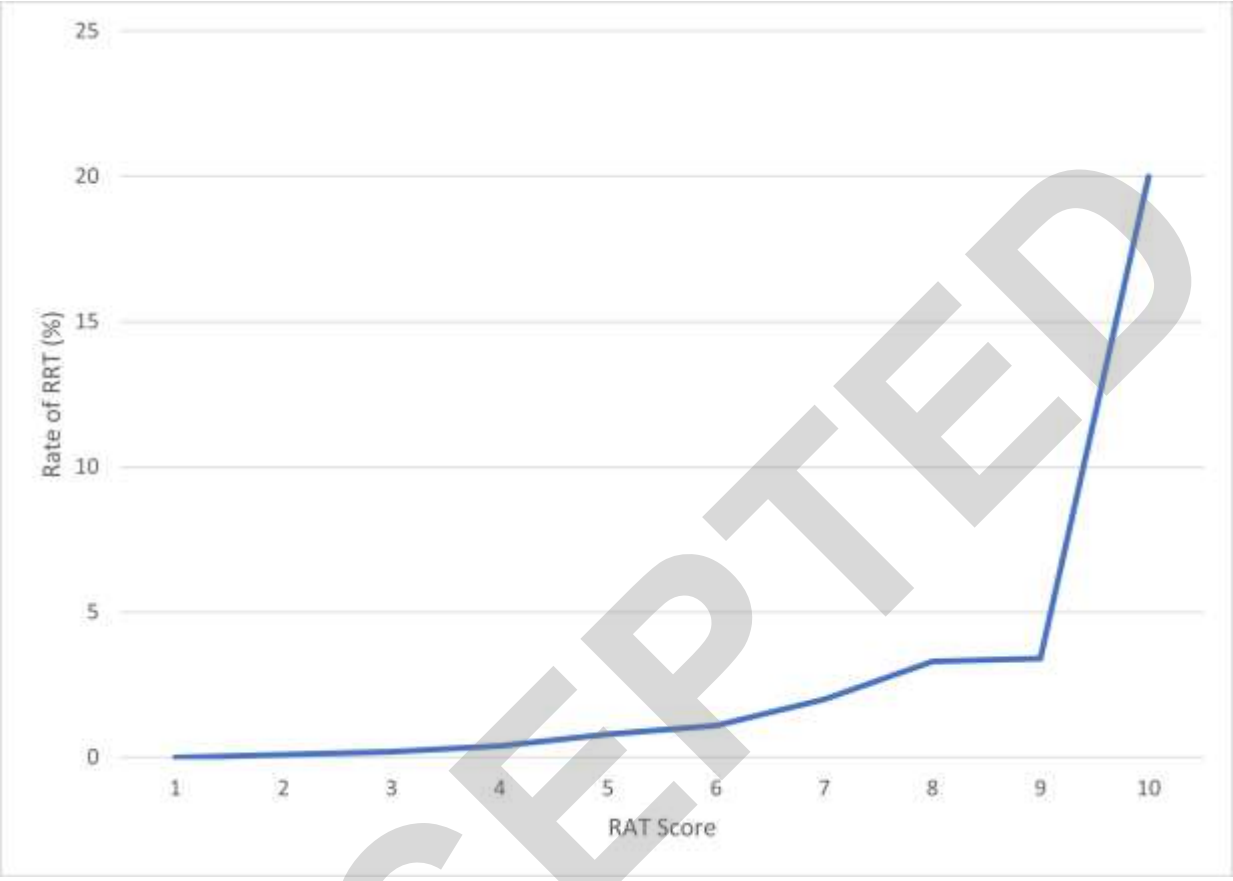

Figure 2