



Association of grit and overall survival in patients undergoing nephrectomy for renal cell carcinoma

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Background: Quantifying grit with the Short Grit Scale (Grit-S) has shown ability to predict success in various academic and professional domains. Grit has yet to be analyzed in patients with cancer.

Methods: This study is a longitudinal analysis of prospectively distributed Grit-S surveys to patients undergoing radical or partial nephrectomy. Patients who completed a preoperative Grit-S survey with confirmed renal cell carcinoma (RCC) were included in the analysis. The relationship between preoperative grit scores and overall survival (OS) was determined using Cox proportional-hazard models and Kaplan-Meier analysis.

Results: A total of 323 patients with RCC that completed the Grit-S survey prior to nephrectomy were included in the study. Median Grit score was 3.9. Most patients were male (67.5%), White (69.3%), and greater than 60 years old (57.0%) with a median age of 62 at the time of surgery. Patients scoring above or below the median grit score had similar baseline characteristics. As a binary variable, lower preoperative grit was significantly associated with shorter OS [hazard ratio (HR) =2.02, 95% confidence interval (CI): 1.12–3.63, P=0.019] on multivariable analysis. Unit changes in grit were not significantly associated with OS (HR =0.77, 95% CI: 0.53–1.14, P=0.193).

Conclusions: Lower grit scores may predict decreased OS in RCC patients undergoing nephrectomy. The Grit-S survey may have utility in preoperative evaluation. Further research assessing grit in other malignancies and how to psychologically optimize patients prior to surgery are needed.

Keywords: Grit; Short Grit Scale (Grit-S); cancer; renal cell carcinoma (RCC); nephrectomy

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Introduction

Psychiatric disorders are highly prevalent in oncologic populations, including patients with renal cell carcinoma (RCC), and may result in detrimental effects on patient outcomes (1-4). Early identification and treatment of psychiatric illnesses such as depression and anxiety has been the traditional focus of psychologically optimizing cancer patients. However, a growing body of research has suggested that positive personality traits may supplement previous strategies through the promotion of healthier behaviors, while simultaneously buffering negative emotions (5). Positive psychosocial traits provide a variety of benefits for medical patients, including improvements in health-related maintenance, treatment compliance, and overall wellbeing (5-11). Grit, defined as passion and perseverance for long-term goals, offers potential advantages to the cancer population, as it denotes an increased ability to overcome adversity (12-17). Unlike resilience, a positive trait that reflects one's immediate capacity to psychologically recover from stressful events, grit allows the individual to withstand emotional disturbances over extended periods while remaining goal-oriented. Furthermore, when compared to patients with lower grit, those with higher levels exhibit an increased capacity to diligently pursue tasks to completion, despite the presence of obstacles or setbacks (6,12-14,16-19).

Much of the research surrounding grit has focused on its ability to predict success and performance in various academic and professional domains. With the Short Grit Scale (Grit-S), a questionnaire used to quantify grit, studies have demonstrated that grit successfully predicts retention among cadets in the United States Military Academy, academic performance in Ivy League schools, resistance to professional burnout, and adherence to regular exercise (8,9,12,13,15,20,21). Moreover, higher levels of grit are associated with reduced depression and anxious symptomatology, as well as improved compliance to physician recommendations in chronically diseased populations (7-9,12,13,21,22).

A diagnosis of RCC often results in considerable psychiatric distress for patients, which may be further amplified when evaluating surgical interventions and other treatment options (23,24). Adequate management of these emotional stressors is variable among patients and ultimately may worsen outcomes when coping strategies are absent (3,21,25). Despite its proven reliability and validity when determining success in academic and professional environments, no studies have examined the utility of the

Grit-S in oncologic or surgical settings. We hypothesize that lower preoperative Grit-S scores will be significantly associated with inferior survival outcomes in RCC patients undergoing partial or radical nephrectomy. We present the following article in accordance with the STROBE reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-22-408/rc>).

Methods

Patients and procedure

This is a retrospective analysis of prospectively collected data from RCC patients who completed a preoperative Grit-S prior to undergoing partial or radical nephrectomy at Emory University, a tertiary academic urologic oncology referral center. We identified patients presenting to the urology clinic for preliminary evaluation of a renal mass. Grit-S questionnaires are routinely provided to patients during their preoperative assessment and are self-administered and completed by the patients during this in-person clinic encounter. Patients who completed the Grit-S within 160 days of undergoing radical or partial nephrectomy and received a histologically confirmed diagnosis of RCC were included in the analysis. If a patient had more than one appointment prior to surgery, and therefore completed multiple surveys, the survey closest to the operation date preoperatively was analyzed. If a survey was inappropriately or incompletely filled out, then the survey was excluded. Other exclusion criteria include respondents with urothelial carcinoma, benign renal masses, and missing clinical data respective to primary exposure and outcome variables chosen in this analysis. Tumors were pathologically staged according to the 2017 tumor, node, metastasis (TNM) staging system for renal tumor classification. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Emory University (No. 00055316) and informed consent was taken from all individual participants.

Measures

Short Grit Form: The Short Grit form is a well-validated and widely used tool for the general population in measuring an individual's grit (13). The Grit-S is an 8-question form, adapted from an original 12-question form, that serves to predict one's perseverance or ability

to work towards long-term goals. The items represent a 5-point Likert scale with each item scored from 1–5. The overall score is calculated in the following manner:

$$\text{Score} = \frac{Q1+Q2+Q5+Q6+(6-Q3)+(6-Q4)+(6-Q7)+(6-Q8)}{8} \quad [1]$$

Higher scores represent higher amounts of grit. The 8-questions evaluate a patient's consistency of interest in the task and perseverance of their effort. These questions evaluate interest in tasks, ability to respond to setbacks, consistency in the face of distraction, how hard one works, ability to complete set goals, and diligence (12,13). Internal consistency was calculated by Cronbach's alpha, which was adequate in this study ($\alpha=0.71$).

Statistical analysis

The primary outcome assessed was overall survival (OS), defined as time from surgery to death from any cause. OS was analyzed using Cox proportional-hazard models and Kaplan-Meier analysis. The primary exposure variable was total Grit-S score, analyzed both as a binary and continuous variable in separate logistic regression models. Patient and disease covariates such as age, race, sex, body mass index (BMI; kg/m²), TNM staging, Eastern Cooperative Oncology Group (ECOG) status, Charlson Comorbidity Index (CCI), Fuhrman grade, and TNM staging were included in the analysis. A binary cut-off value of 3.9, developed from the median Grit-S score in our cohort (3.9, Min–Max: 1.8–5), was used to distinguish those with high versus low grit, as there are no pre-established cutoffs validated in the literature. Uni- and multivariable logistic regression models were fit. Statistically significant covariates in univariable analysis were selected for inclusion in multivariable analysis after interaction assessment and collinearity testing. Multivariable models were adjusted for age, race, sex, BMI, ECOG status, CCI, and TNM staging. All statistical tests were two-sided with type I error set at 0.05. All analyses were performed using SAS version 9.4 (Cary, NC, USA).

Results

Table 1 demonstrates the baseline characteristics of our cohort. Three hundred and twenty-three patients who completed the Grit-S between September 2011 and December 2020 prior to radical or partial nephrectomy were included in the study. The median time from

preoperative survey completion to surgery was 43 days. The median follow up time was 23.5 months. Of note, the majority of patients were male (67.5%), White (69.3%), and greater than 60 years old (57.0%) with a median age of 62 at the time of surgery. Overall, most patients were fully active with the ability to perform activities of daily living (ECOG 0; 86.4%). The relatively high rate of T3–T4 stage tumors (52.7%) seen in our sample population likely reflects referral trends to our institution. Furthermore, most patients had neither nodal involvement (88.7%) nor metastasis (78.7%). The majority of our cohort were categorized as low grit indicated by Grit-S scores below the median of 3.9 (54.5%). The only missing data in this analysis was Fuhrman grade for 16 patients. There were no baseline characteristic differences between those with low and high grit. Analysis was completed to identify any possible associations between grit and the other covariates with no significant associations identified.

Kaplan-Meier survival curves displayed a statistically nonsignificant decrease in OS time among RCC patients who scored <3.9 on the Grit-S ($P=0.1205$) (*Figure 1*). OS rates at 36 months after nephrectomy for patients with a Grit-S score <3.9 and ≥ 3.9 were 74.4% and 79.9%, respectively.

On univariable analysis (*Table 2*), age, ECOG ≥ 1 , CCI, T3/4, N1, M1, and Fuhrman grade 3–4 were significantly associated with decreased OS. Low Grit trended towards lower OS on univariable analysis, but this was not significant.

The results from multivariable analysis are shown in *Table 3*. In the OS multivariable model, ECOG ≥ 1 , pathologic T4 stage disease, and the presence of metastasis were significantly associated with decreased OS. Nodal involvement was not significantly associated with decreased OS in this specific cohort. Notably, lower preoperative grit scores were significantly associated with decreased OS (HR =2.02, 95% CI: 1.12–3.63, $P=0.019$). However, unit increases or decreases in Grit-S were not significantly associated with OS (HR =0.77, 95% CI: 0.53–1.14, $P=0.193$).

Discussion

The current study aims to evaluate the role of grit in RCC patients scheduled for radical or partial nephrectomy, specifically concerning OS. When analyzed as a binary variable, we observed lower preoperative grit scores to be significantly associated with decreased OS (HR =2.02,

Table 1 Comparison of baseline characteristics between patients with low and high Grit scores

| Characteristic | All patients (n=323) | Below median (n=176) | Above median (n=147) | P value |
|--|----------------------|----------------------|----------------------|---------|
| Age (years), median (IQR) | 62.2 (29.4–89.9) | 61.6 (29.4–89.9) | 63.9 (34.7–84.6) | 0.355 |
| Sex, n (%) | | | | 0.959 |
| Female | 105 (32.5) | 57 (32.4) | 48 (32.7) | |
| Male | 218 (67.5) | 119 (67.6) | 99 (67.3) | |
| Race, n (%) | | | | 0.126 |
| White | 224 (69.3) | 123 (69.9) | 101 (68.7) | |
| Black | 81 (25.1) | 39 (22.2) | 42 (28.6) | |
| Other | 18 (5.6) | 14 (8.0) | 4 (2.8) | |
| Obesity (≥ 30 kg/m ²), n (%) | | | | 0.856 |
| Yes | 149 (46.1) | 82 (46.6) | 67 (45.6) | |
| ECOG Performance Score, n (%) | | | | 0.332 |
| 0 | 279 (86.4) | 155 (88.1) | 124 (84.4) | |
| ≥ 1 | 44 (13.6) | 21 (11.9) | 23 (15.6) | |
| CCI, n (%) | | | | 0.200 |
| 0–3 | 116 (35.9) | 60 (34.1) | 56 (38.1) | |
| 4+ | 207 (64.1) | 116 (65.9) | 91 (61.9) | |
| Pathologic T stage, n (%) | | | | 0.341 |
| pT1 | 134 (41.5) | 73 (41.5) | 61 (41.5) | |
| pT2 | 19 (5.9) | 13 (7.4) | 6 (4.1) | |
| pT3 | 154 (47.7) | 84 (47.7) | 70 (47.6) | |
| pT4 | 16 (5.0) | 6 (3.4) | 10 (6.8) | |
| Pathologic N stage, n (%) | | | | 0.556 |
| N0 | 266 (88.7) | 155 (88.6) | 131 (89.1) | |
| Pathologic M stage, n (%) | | | | 0.877 |
| M0 | 236 (78.7) | 135 (76.7) | 121 (82.3) | |
| Fuhrman grade, n (%) | | | | 0.886 |
| 1–2 | 71 (23.13) | 38 (22.8) | 33 (23.6) | |
| 3–4 | 236 (76.67) | 129 (77.2) | 107 (76.4) | |
| Grit Score | | | | |
| Median (min–max) | 3.9 (1.8–5) | | | |
| Above median, n (%) | 147 (45.5) | | | |
| Below median, n (%) | 176 (54.5) | | | |

ECOG, Eastern Cooperative Oncology Group; CCI, Charlson Comorbidity Index.

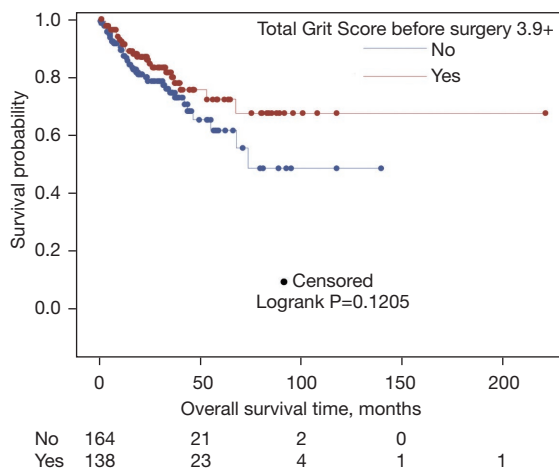


Figure 1 Kaplan-Meier survival curve displaying association between overall survival time and total Grit Score.

95% CI: 1.12–3.63, P=0.019) in multivariable analysis after adjustment for TNM staging and other factors, however, this association was not statistically significant in the univariable model. Analysis of grit scores as a continuous variable revealed a potential protective influence on OS, albeit not being statistically significant (HR =0.77, 95% CI: 0.53–1.14, P=0.193). These results suggest Grit-S may have prognostic utility and assist in preoperative risk assessment.

To our knowledge this is the first study to establish an association between low grit and decreased OS in any cancer population undergoing surgical intervention, let alone RCC. Previous clinical analyses have focused on examining the ability of one’s grit to facilitate positive lifestyle modifications in noncancerous cohorts. Peña *et al.* observed type II diabetics with higher Grit-S scores to have greater adherence to medications, diet, and exercise, which ultimately resulted in superior laboratory measures of disease control (8). Moreover, two individual studies demonstrated associations with higher grit and propensity to exercise among Parkinson’s disease patients, as well as ability to minimize substance abuse and other risky behaviors in adolescents (9,26). Additionally, higher levels of grit have been associated with reduced professional burnout and higher perceived psychological well-being (18,27,28).

Table 2 Univariable analysis of overall survival

| Characteristic | Hazard ratio (95% CI) | P value |
|----------------------------------|-----------------------|---------|
| Age (years) | 1.03 (1.01–1.06) | 0.007* |
| Sex | | |
| Male | 1.07 (0.63–1.84) | 0.796 |
| Female | – | – |
| Race | | |
| Black | 0.58 (0.31–1.12) | 0.101 |
| Obesity (≥30 kg/m ²) | | |
| Yes | 1.16 (0.63–1.84) | 0.553 |
| ECOG Performance Score | | |
| ≥1 | 3.08 (1.77–5.39) | <0.001* |
| CCI | | |
| 0–3 | 0.15 (0.06–0.37) | <0.001* |
| 4+ | – | – |
| Pathologic T stage | | |
| pT1 | – | – |
| pT2 | 2.93 (0.78–11.05) | 0.113 |
| pT3 | 6.07 (2.85–12.94) | <0.001* |
| pT4 | 16.31 (5.78–46.02) | <0.001* |
| Pathologic N stage | | |
| N1 | 3.43 (1.99–5.92) | <0.001* |
| Pathologic M stage | | |
| M1 | 7.42 (4.49–12.26) | <0.001* |
| Fuhrman grade | | |
| 1–2 | – | – |
| 3–4 | 4.49 (1.78–11.33) | <0.001* |
| Total Grit Score | 0.81 (0.57–1.13) | 0.215 |
| Grit Score, binary | | |
| Below median | 1.49 (0.90–2.46) | 0.123 |
| Above median | – | – |

*, statistically significant (P<0.05). ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; CI, confidence interval; CCI, Charlson Comorbidity Index.

Table 3 Multivariable analysis (n=323)

| Characteristic | Hazard ratio (95% CI) | P value |
|---|-----------------------|---------|
| Age (years) | | |
| 60+ | 1.61 (0.86–2.99) | 0.134 |
| Sex | | |
| Male | 0.68 (0.36–1.27) | 0.228 |
| Female | – | – |
| Race | | |
| Black | 1.17 (0.53–2.58) | 0.697 |
| Obesity (≥ 30 kg/m ²) | | |
| Yes | 1.17 (0.64–2.11) | 0.612 |
| ECOG Performance Score | | |
| ≥ 1 | 2.56 (1.30–5.05) | 0.007* |
| CCI | | |
| 0–3 | 0.23 (0.05–1.04) | 0.056 |
| 4+ | – | – |
| Pathologic T stage | | |
| pT1 | – | – |
| pT2 | 1.96 (0.43–8.95) | 0.387 |
| pT3 | 1.92 (0.62–5.96) | 0.258 |
| pT4 | 6.32 (1.57–25.41) | 0.009* |
| Pathologic N stage | | |
| N1 | 1.14 (0.57–2.25) | 0.716 |
| Pathologic M stage | | |
| M1 | 3.86 (2.02–7.37) | <0.001* |
| Fuhrman grade | | |
| 1–2 | – | – |
| 3–4 | 2.19 (0.71–6.77) | 0.174 |
| Total Grit Score | 0.77 (0.53–1.14) | 0.193 |
| Grit Score | | |
| Below median | 2.02 (1.12–3.63) | 0.019* |
| Above median | – | – |

*, statistically significant (P<0.05). ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; CI, confidence interval; CCI, Charlson Comorbidity Index.

Adoption of positive lifestyle modifications that individuals with higher grit exhibit, such as diet, exercise, medication adherence, and increased emotional capacity, has the potential to positively influence survival in patients with cancer (29–32). Conversely, cancer patients with lower grit may be less inclined to adopt and maintain healthier habits and experience lower perceived well-being, potentially explaining the decreased OS among low grit patients observed in our study. Similarly, patient predispositions for healthier behaviors and increased emotional capacity offers a potential rationale for the non-significant relationship between increased OS with graded increases in grit score.

Grit may be protective against psychological low-wellbeing. In a large meta-analysis, depression and anxiety in cancer patients have been identified as risk factors for increased cancer-specific and all-cause mortality (33). A cross-sectional study among healthy university students found that participants with higher scores on the Grit-S scored lower on the Patient Health Questionnaire-9, suggesting those with grit to have a stronger ability to cope with depressive symptoms (21). Further, In Sharkey *et al.*'s research involving grit and chronically diseased patients revealed that higher Grit-S scores were significantly associated with decreased depressive and anxious symptomatology and increased emotional well-being (7,27). These findings further support the claim that grit may be protective against depressive and anxious symptoms. They also suggest that higher levels of grit convey the capability to promote positive psychological adjustments.

Assessing grit in the clinical setting may identify patients at risk for worse outcomes and provide an avenue for pretreatment intervention. Traditional psychological interventions (i.e., psychotherapy) may theoretically improve grit given the possible inverse relationship between grit and anxiety/depressive symptoms. Furthermore, interventions aimed at increasing one's grit are of great interest. However, research looking into these measures is still in its infancy. Grit is influenced by many aspects, such as cultural tendencies, past experiences, upbringing, and personality type; however, evidence exists that Grit may be elastic and subject to improvement (34). Increasing maturity, development, and improved executive function have been linked to improved grit (34). Several strategies

aimed at improving grit have been proposed, including character education programs, emotional regulation, growth mindset, reflection/writing on failures, mentoring programs, and deliberate practice (34). Future studies regarding grit development and its impact on physical and mental health outcomes are of clinical interest.

In logistic regression analysis evaluating grit as a binary variable, we found lower grit conveyed a statistically significant decrease in OS when compared to patients with high grit; however, though we saw the same trend in univariable analysis, this was not statistically significant. Statistical scenarios such as unbalanced sample size, influence of missing data, large within group variation, and the influence of confounders or interaction effects are known to contribute to the discordance of results in univariable against multivariable regression analysis. Due to the modest sample size in the present analysis, particularly for a survey-based study, there is limited ability to fully appreciate differences in all of the tested parameters. Prospective controlled studies with inclusion of multiple timepoints of surveys assessing patients' mental health status are needed to further evaluate the role of grit in predicting survival in RCC populations.

There were several in this study. The retrospective study design inhibits our ability to establish causation. Our sample population of 300 is relatively small for a survey-dependent study and a larger sample size would allow for a more detailed analysis of the nature of the relationship between Grit and OS. Only including RCC patients may limit generalizability of these results, though we believe core concepts apply to various oncology and surgical populations. The lack of validated Grit-S cutoffs limits analysis. Furthermore, we did not control for life events outside of their cancer diagnosis that may have influenced their grit score, such as psychological conditions and physical, emotional, or financial stress. Due to the absence of prior analysis of grit's effects on cancer related outcomes, we relied on background information and comparisons to studies unrelated to cancer or survival outcomes.

Finally, the setting of a tertiary referral center allowed us to evaluate a large number of high-risk RCC (>50% T3/T4) patients, which has some strengths and limitations. We had the unique opportunity to gain insight into a group of patients with higher risks of postoperative morbidity and mortality, who arguably stand to benefit the greatest from preoperative behavioral modification and intervention. However, this higher risk population may also result in some selection bias of the results. Furthermore, follow-

up time was limited due to status as a referral center as patients may choose to follow with personal physicians and urologists closer to home.

Future studies regarding Grit in patients with RCC and other malignancies are encouraged. Study cohorts with more common, lower risk RCC cases would be of interest. In addition to further elucidating the relationship of grit and OS, other survival analyses, such as cancer specific survival, should be conducted. Psychiatric comorbidities in relationship to grit and cancer outcomes should be considered.

Conclusions

Advances in the surgical management of RCC have led to increased interest in understanding how psychological states influence surgical and survival outcomes in patients undergoing nephrectomy. This requires a reliable, evidence-based method to identify patients that may need psychological optimization prior to surgery. Our study found that lower grit scores may be an independent predictor of decreased OS in RCC patients undergoing nephrectomy. The present study provides evidence to encourage research on Grit-S in other malignancies in the preoperative evaluation and how to psychologically optimize patients preoperatively.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tau.amegroups.com/article/view/10.21037/tau-22-408/rc>

Data Sharing Statement: Available at <https://tau.amegroups.com/article/view/10.21037/tau-22-408/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tau.amegroups.com/article/view/10.21037/tau-22-408/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Emory University (No. 00055316) and informed consent was taken from all individual participants.

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