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The QuantiFERON Monitor® Assay is predictive of infection post allogeneic hematopoietic cell transplant.

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Qiagen Inc., Valencia, USA provided the necessary equipment and funded laboratory worker time for performance of the QFM assay. They were not involved in data collection, data analysis and interpretation or production of the manuscript.

LY was a former employee of Qiagen Inc. prior to her involvement in this study.

Abstract

Following allogeneic haematopoietic stem cell transplantation (alloHCT), excessive immunosuppression can be complicated by infection, while inadequate immunosuppression can result in graft versus host disease (GVHD). An accurate method to assess overall immune status post HCT is lacking. The QuantiFERON Monitor® (QFM) assay measures interferon gamma (IFN- γ) release from whole blood following incubation with both innate (Toll Like Receptor 7, TLR7) and adaptive (CD3- antibody) stimulants and may result in a more complete assessment of the immune system.

Whole blood samples were prospectively collected from alloHCT recipients at conditioning followed by days 10, 30, 60, 90, 120 and 180 post-transplant and assayed by the QFM test. IFN- γ levels were correlated to time post HCT, episodes of infection and GVHD.

Forty patients were enrolled in the study (68% male; median age 47 years; 58% matched-related donors, 42% unrelated; 33% myeloablative). Post-stimulation IFN- γ

levels rose steadily over the first 180 days post transplantation. IFN- γ levels were significantly lower in those with active infection compared to those without during the neutropenic period ($p < 0.001$). The assay was predictive of CMV reactivation (VL > 1000 copies/ml) post alloHCT ($p = 0.001$).

This is a promising assay to demonstrate immune recovery and predict risk of infection after alloHCT and may allow tailoring of immunosuppression, antimicrobial treatment and prophylaxis.

Introduction

Allogeneic haematopoietic stem cell transplantation (alloHCT) can be a life-saving intervention for those with hematologic malignancy and other incurable hematologic disorders. There is, however, potential for significant morbidity and mortality due to infection and graft versus host disease (GVHD). Identifying the balance of immunosuppression between infection (excessively immunosuppressed) and GVHD (insufficient immunosuppression) can be challenging. Accurate risk prediction based on clinical parameters is complex ^{1,2}. Currently, tests that assess immune reconstitution and hence risk of infection consist primarily of lymphocyte subset analyses and immunoglobulin levels. These are not functional tests and may not accurately measure immune recovery ³. There is therefore an unmet need for a non-invasive, simple test to help predict or detect the early development of infection and GVHD and help titrate the immunosuppression required to avoid toxicities and infections.

The QuantiFERON Monitor[®] assay (QFM, Qiagen Inc., Valencia, USA) has the potential advantage of assessing both adaptive and innate immune activity components in a patient at a point in time. It measures interferon-gamma (IFN- γ) production in plasma after incubation of heparinized whole blood with innate (R848, a TLR7 agonist) and adaptive (CD3 antibody) stimulants. It is a straightforward assay that requires minimal technical expertise to execute, with results available in real time within a day. The potential benefits of the assay have been previously examined in liver transplant recipients, where there was a demonstrated increase in IFN- γ production over time post transplant, which would be expected with increasing immunologic recovery and weaning immunosuppression ⁴, and there has been a correlation shown between assay levels and infection post solid organ transplant ⁵. As

yet, there has been no prospective evaluation of this assay in alloHCT patients.

This study aimed to monitor IFN- γ levels using the QFM assay in alloHCT patients over the course of their transplant to profile immune recovery and correlate results with episodes of infection and GVHD. We hypothesised that IFN- γ levels would be lower in those who are relatively more immunosuppressed and therefore be more susceptible to infections and that IFN- γ levels would be higher, indicating immune activation, in those with GVHD.

Methods

Patients and study design

This was a prospective, single-centre study of patients undergoing alloHCT, with all patients recruited from the bone marrow transplantation service at Royal Melbourne Hospital, a tertiary hospital in Melbourne, Australia. Study patients were identified and enrolled by the transplant coordinator as they were approaching their alloHCT between May 2014 and October 2015. All patients were >18yrs of age, having their first alloHCT and provided written, informed consent. There were no specific exclusion criteria. This research project was approved by the Human Research Ethics Committee of Melbourne Health.

Clinical assessment and laboratory testing time points

Whole blood samples were collected from 40 alloHCT recipients at enrolment (“baseline”), immediately prior to conditioning (“pre-conditioning”) and on day 10 (mid neutropenia), 30, 60, 90, 120 and 180 post alloHCT. An infectious or GVHD episode was ascribed to the sample timepoint that predated the episode, for example, an infectious episode that occurred on day 40 was ascribed to the day 30 result.

Baseline clinical information including demographics, type of transplant, conditioning regimen, CMV sero-status and GVHD prophylaxis was collected for each subject on enrolment. Follow up prospective clinical information was collected at each testing time point; this included presence of GVHD (site, method of diagnosis), the presence

of infections, CMV reactivation, serum neutrophil and lymphocyte counts, doses of immunosuppressing agents and any relapse of underlying disease. Infection was defined as an illness with a clinically suspected +/- microbiologically defined infectious aetiology necessitating hospital admission (not including CMV reactivation, which was analysed separately). Culture negative neutropenic fever (fever ≥ 38 degrees with neutrophil count $\leq 0.5 \times 10^9/L$) was recorded as a clinically suspected infection without confirmed aetiology. CMV reactivation was defined as a CMV DNA load of >1000 copies/ml in plasma on weekly surveillance (Realtime CMV Assay, Abbott Molecular, USA) and the association with IFN- γ levels were analysed separately. The CMV DNA cut off of >1000 copies/ml was utilised as it is the threshold at which pre-emptive therapy is routinely initiated at our centre.

The presence of GVHD was determined by the treating physician, based on clinical, and/or histologic findings. Acute GVHD was defined as GVHD diagnosed <100 days post transplant, with chronic GVHD defined as all episodes of GVHD diagnosed thereafter. For the purposes of the analysis, severity of GVHD was grouped into those not requiring treatment or those requiring institution of new treatment.

Antifungal, PJP and antiviral prophylaxis was prescribed according to unit policy. In brief, all HCT recipients received valaciclovir or acyclovir throughout the transplant period until at least 12 months post transplant, and cotrimoxazole was commenced on count recovery until 12 months post transplant. Antifungal prophylaxis was with either fluconazole or voriconazole depending on risk profile, which was typically ceased at day 100 unless GVHD was evident, whereby prophylaxis was continued until immunosuppression was no longer required. Fluoroquinolone prophylaxis was not used. CMV nucleic acid detection was performed weekly until day 100 and pre-emptive therapy was used.

Laboratory evaluation

Whole blood collection was undertaken at Royal Melbourne Hospital with samples transported to the Immunology Research Centre, St. Vincent's Hospital Melbourne for processing of the QFM assay (Qiagen Inc., Valencia, USA) performed by trained laboratory personnel. In brief, 1mL of heparinized whole blood was stimulated within

8 hours of being taken using the QFM stimulants in a lyophilized sphere containing R848 and CD3 antibody. Samples were incubated for 16 to 24 hours at 37°C and plasma was then harvested following centrifugation of the blood incubation tubes. The IFN- γ (IU/mL) level in the plasma was measured using the QFM ELISA kit (Qiagen Inc., Valencia, USA).

Statistical analyses

Differences between IFN- γ values against all the groups measured were compared using non-parametric significance tests (Wilcoxon- Rank Sum (2 groups), Kruskal Wallis test (more than two groups)). A Spearman's Rank correlation coefficient was employed to test the correlation between IFN- γ values and neutrophil and lymphocyte counts. Two multiple logistic regression models were fitted to estimate the independent association of IFN- γ levels to infective episodes at the peak times of day 10 and engraftment after adjusting for neutrophil and lymphocyte count. A p value of <0.05 was considered significant. All statistics were performed using the Stata statistical package- version 13.0.

Results

Forty patients were recruited and followed over the first 180 days following alloHCT between May 2014 and October 2015. **Table 1** describes the baseline characteristics of the cohort. Sixty-eight per cent of patients were male, half of the patients were transplanted for acute myeloid leukaemia, and two-thirds received a reduced intensity conditioning regimen (67%). The majority of patients received cells from a peripheral blood stem cell source, and approximately half of recipients (58%) were from a matched related donor. At each time point, IFN- γ levels did not vary with sex, donor age, donor source (matched-related versus unrelated), conditioning regimen (myeloablative versus reduced intensity) or receipt of T-cell depleting agents (data not shown). IFN- γ levels rose steadily over the first 180 days post transplantation (**Figure 1**) although levels had not returned to baseline by day 180. Age was stratified to young (<35 yrs), middle age (35-55 yrs) and old (>55 yrs). There was a trend for IFN- γ levels to be higher in younger compared to older recipients up until day 120 post transplant, although this did not reach statistical significance (**Figure 2**).

Correlation with leucocyte indices

The correlation co-efficient between IFN- γ levels and neutrophil count at any time post-transplant was 0.14, suggesting a poor correlation ($p=0.056$). The correlation co-efficient between IFN- γ levels and lymphocyte count was better and significant at 0.59 ($p<0.001$).

Correlation with episodes of infection

Sixty-three episodes of suspected or confirmed infection occurred in 38 patients, with 60 identified causative organisms in 52 episodes of confirmed infection and 11 episodes without an identified organism. Of the causative organisms identified, 18 were viral, 39 bacterial and 3 were of presumed fungal aetiology (**Table 2**). The three fungal infections were all possible invasive fungal respiratory infections based on radiologic findings according to EORTC/MSG criteria ⁶. IFN- γ levels varied significantly between those with active infection and those without, with higher levels in the absence of infection at a particular timepoint (median 93.4 IU/ml [IQR 8.8-621.5]) and lower levels during an infective episode (median 55.6 IU/ml [IQR 2.4-81.6]) ($p<0.001$) (**Figure 3a**). In the sub-analysis restricted to microbiologically-defined infections only, there remained a statistically significant relationship between IFN- γ levels and infection at a particular timepoint ($p<0.001$) (Figure 3b).

When separating the analysis into neutropenic and non-neutropenic phases, in an analysis incorporating neutrophil and lymphocyte counts as covariates, there remained a statistically significant relationship between IFN- γ levels and infective episodes during the neutropenic/pre-engraftment period (day 10) (**Table 3**). Infective episodes were very infrequent beyond engraftment (**Figure 4**) and there was no statistically significant relationship between IFN- γ levels and infection at or following engraftment (day 30).

Twenty-four patients had a detectable CMV viraemia during the first 180 days post-transplant. One patient developed CMV colitis at day 90 post-transplant. There was no significant difference in IFN- γ levels at a particular timepoint between those

patients with and without any detectable CMV viraemia, however IFN- γ levels were significantly lower in those with CMV viral load >1000 at that timepoint (median 3.3 IU/ml [IQR 1.7-31]) (11 patients, 13 timepoints) compared to those with a load <1000 or undetectable (29 patients, 240 timepoints) (median 164.5 [IQR 16.2-715]) ($p=0.001$) (**Figure 5**).

Correlation with GVHD

Nine patients required an increase of immunosuppression for acute GVHD treatment. Eleven patients required escalation of immunosuppression for chronic GVHD treatment. There was no statistically significant difference in IFN- γ levels in the blood draw prior to aGVHD diagnosis and treatment (median 5.02 [range 0.02-1818]), compared to the blood draw following commencement of treatment for aGVHD (median 8.8 [range 0.02-79]) ($p=0.88$) (Figure 6A). There was also no statistically significant difference between cGVHD and IFN- γ levels (Figure 6B), ($p=0.21$ for three-way comparison between groups).

Discussion

This study is the first in the alloHCT group prospectively utilising this unique assay that assesses both innate and adaptive immune activity. In this pilot prospective assessment of changes in IFN- γ release in alloHCT patients, the most striking finding was the ability of the QFM assay to predict infection during the neutropenic/pre-engraftment phase. Whilst the odds ratio for risk of infection may not seem great (0.96), this is per unit of the assay (IU/ml), and with assay levels varying from zero up to several thousand, this suggests a substantial correlation between QFM assay levels and infection risk. Lower QFM assay levels suggest that the patient is more likely to suffer from infection. We recognise that there are other factors unaccounted for that may place a patient at risk of infection, such as central line placement, mucositis and treatment for GVHD, however this is a pilot study assessing the overall performance of the test, and there was not the power to examine such relationships in detail. Larger prospective studies with more detailed timepoint testing would be the logical next step to further explore the relationship between assay levels and infection.

There is likely a simple explanation for our inability to detect an association between the QFM assay and infection post-engraftment. The numbers of infective episodes were low in this cohort post-engraftment, most likely due to ongoing PJP prophylaxis with cotrimoxazole, as well as anti-herpetic antiviral (acyclovir/valacyclovir) and mould-active antifungal prophylaxis. It is therefore likely that this study was underpowered to assess this relationship in this setting. We did, however, see a negative relationship between clinically significant CMV reactivation and the assay levels. Unlike other infective etiologies, CMV infection post-allograft was not managed with routine prophylaxis but rather with a pre-emptive therapy approach where viral reactivation occurred prior to the introduction of therapy ⁷, offering an opportunity for the relationship between CMV reactivation and the QFM assay to be explored in this study. It appears promising that we may be able to identify those at higher risk of CMV reactivation and potentially CMV disease (namely those with low QFM levels) and monitor them more closely, provide prophylaxis or consider earlier pre-emptive therapy at lower viral loads. This finding also adds weight to the notion that the QFM assay is identifying those with a low net immune state as it correlates with those who experienced viral reactivation.

There was an unsurprisingly poor correlation between neutrophil count and IFN- γ levels, however, the stronger correlation between lymphocyte counts and IFN- γ levels is logical, as natural killer cells, natural killer T cells and T cells produce IFN- γ in response to infection. The correlation is not perfect however and did not account for all variation observed in the multivariate analysis for prediction of infection, which suggests that the QFM assay is likely measuring the activity of other cells in the immune milieu such as macrophages and dendritic cells, providing a more holistic view of the net immune state. In other words, this assay offers more in predicting infection than monitoring the lymphocyte count alone.

Overall IFN- γ levels rose steadily over time post alloHCT. Indeed, even at 180 days post-transplant, immune function had still not returned to baseline and pre-conditioning levels. This reflects both immune recovery post-transplant, and the progressive weaning of GVHD prophylaxis. It was notable that patient sex, donor source (between matched related and unrelated), T cell depletion and the intensity of the conditioning regimen did not influence IFN- γ levels, therefore reducing the

number of factors to be accounted for when interpreting the test in an individual patient. This test therefore could potentially be applied in the clinic to assess the net state of immunosuppression in a patient post alloHCT and aid in individual tailoring of prophylaxis initiation, continuation and its safe cessation. Lower assay levels may also be a signal of excessive immunosuppression, and down-titration of immunosuppressing medications used for GVHD prophylaxis could mitigate the risk of infection. This pilot study shows the potential promise of the QFM assay in predicting infection post alloHCT, however further more detailed studies are required to explore this potential further.

Assay levels and GVHD

Given the low numbers of GVHD, the study was underpowered to detect any statistically significant association between acute or chronic GVHD and the QFM assay. Furthermore, the low numbers limited the ability to account for any confounders in this relationship. A larger study would be required to explore any potential relationship further.

Limitations

This is a pilot study assessing possible relationships between QFM assay results, GVHD and infection. Larger studies are required to fully elucidate relationships and establish cut-off values for practical use in the clinic that would signify a risk of infection. In addition, results cannot be extrapolated to haploidentical and cord blood patients as, at the time of performance of the study, there were few such donors utilized at our centre. Assessing what impact these alternative donors have on the QFM assay would be important, given the different immune recovery profiles of these alternative transplants^{3,8}. Finally, immune function in later phases of an alloHCT has not been explored in this study, however a cross-sectional study assessing IFN- γ levels in QFM assay at later time-points post-transplant is currently underway at our centre.

Conclusions

In this pilot study, IFN- γ levels as measured by the QFM assay steadily increased over the first 180 days post alloHCT and lower levels correlated with overall risk of

infection during the pre-engraftment period suggesting a predictive nature of the test to identify those with an infection. Lower IFN- γ levels also correlated with CMV reactivation, which may have implications for closer clinical monitoring and initiation of pre-emptive or prophylactic CMV therapy. Larger studies with more frequent testing would be required to confirm these findings and identify useful cut offs for clinical use.

References

1. Girmenia C, Raiola AM, Piciocchi A, et al. Incidence and outcome of invasive fungal diseases after allogeneic stem cell transplantation: a prospective study of the Gruppo Italiano Trapianto Midollo Osseo (GITMO). *Biol Blood Marrow Transplant*. 2014;20(6):872-880.
2. George B, Pati N, Gilroy N, et al. Pre-transplant cytomegalovirus (CMV) serostatus remains the most important determinant of CMV reactivation after allogeneic hematopoietic stem cell transplantation in the era of surveillance and preemptive therapy. *Transpl Infect Dis*. 2010;12(4):322-329.
3. Gesundheit B, Budowski E, Israeli M, et al. Assessment of CD4 T-lymphocyte reactivity by the Cylex ImmuKnow assay in patients following allogeneic hematopoietic SCT. *Bone Marrow Transplant*. 2010;45(3):527-533.
4. Sood S, Cundall D, Yu L, et al. A novel biomarker of immune function and initial experience in a transplant population. *Transplantation*. 2014;97(8):e50-51.
5. Mian M, Natori Y, Ferreira V, et al. Evaluation of a Novel Global Immunity Assay to Predict Infection in Organ Transplant Recipients. *Clin Infect Dis*. 2018;66(9):1392-1397.
6. De Pauw B, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. *Clin Infect Dis*. 2008;46(12):1813-1821.
7. Ljungman P, de la Camara R, Cordonnier C, et al. Management of CMV, HHV-6, HHV-7 and Kaposi-sarcoma herpesvirus (HHV-8) infections in patients

with hematological malignancies and after SCT. *Bone Marrow Transplant*. 2008;42(4):227-240.

8. Mehta RS, Rezvani K. Immune reconstitution post allogeneic transplant and the impact of immune recovery on the risk of infection. *Virulence*. 2016:1-16.

Author's contributions:

JSz, DR, MS, JSa and KV participated in research design.

AD collected patient data.

LY performed the assays.

AD, LY, VS, JSa and KV participated in data analysis.

All authors were involved in interpreting the data and writing the manuscript.

Table 1: Baseline characteristics of study population

Variable	Number of patients (%) or median (range) (n=40)
Age (years)	47 (18-69)
Male sex	27 (68%)
Diagnosis	
- Acute myeloid leukemia	20 (50%)
- Multiple myeloma	8 (20%)
- Myelodysplastic syndrome	6 (15%)
- Other†	6 (15%)
Type of transplant	
- Matched related	23 (58%)
- Matched unrelated	17 (42%)
Stem cell source	
- Peripheral blood	38 (95%)
- Bone marrow	2 (5%)
Pretransplantation conditioning	
- Myeloablative	13 (33%)

- Reduced intensity	27 (67%)
CMV status	
- D+R+	20 (50%)
- D+R-	5 (13%)
- D-R-	6 (15%)
- D-R+	9 (22%)
GVHD prophylaxis	
- Cyclosporine [‡]	40 (100%)
- Methotrexate	15 (38%)
- Prednisolone	8 (20%)
- ATG	17 (43%)
- Tocilizumab	3 (8%)

CMV- cytomegalovirus, GVHD- graft versus host disease, ATG- antithymocyte globulin.

† Other diagnoses: 2 of aplastic anaemia; 1 of chronic myelocytic leukemia, diffuse large B-cell lymphoma, X-linked chronic granulomatous disease, chronic lymphocytic leukemia.

‡ Cyclosporine was weaned progressively over the first 100 days of the transplant in the absence of GVHD.

Table 2: Viral and bacterial infections recorded during study, excluding CMV reactivation

Viral infections		Bacterial infections	
Respiratory	7	Blood	20
• Rhinovirus	4	• <i>Klebsiella/raoultella</i> sp.	3
• RSV	1	• <i>Klebsiella pneumoniae</i>	3
• Influenza	1	• <i>Serratia marcescans</i>	2
• Unspecified URTI	1	• <i>Pseudomonas aeruginosa</i>	2
Gastrointestinal	1	• <i>Streptococcus mitis</i>	2
• Rotavirus	1	• <i>Staph. epidermidis</i>	2
Central nervous system	1	• <i>Enterobacter cloacae</i>	1
• Herpes simplex virus	1	• <i>Escherichia coli</i>	1
Urinary tract	6	• <i>Leptotrichia trevisanii</i>	1
• BK virus	6	• <i>Enterococcus faecium</i>	1

Systemic	3	<ul style="list-style-type: none"> <i>Staphylococcus aureus</i> 	1
<ul style="list-style-type: none"> EBV reactivation 	3	<ul style="list-style-type: none"> <i>Streptococcus salivarius</i> 	1
		Gastrointestinal	8
		<ul style="list-style-type: none"> <i>Clostridium difficile</i> 	8
		Urinary tract infection	3
		<ul style="list-style-type: none"> <i>Escherichia coli</i> 	2
		<ul style="list-style-type: none"> <i>Klebsiella pneumoniae</i> 	1
		Line infection	3
		<ul style="list-style-type: none"> <i>Acinetobacter ursingii</i> 	1
		<ul style="list-style-type: none"> <i>Staphylococcus aureus</i> 	1
		<ul style="list-style-type: none"> <i>Staphylococcus capitis</i> 	1
		Respiratory tract	3
		<ul style="list-style-type: none"> <i>Staph. haemolyticus</i> 	1
		<ul style="list-style-type: none"> <i>Pseudomonas aeruginosa</i> 	1
		<ul style="list-style-type: none"> Pneumonia unspecified 	1
		Necrotising fasciitis	1
		Bacterial sinusitis	1

Sp.- species; RSV- respiratory syncytial virus; URTI- upper respiratory tract infection; EBV- Epstein Barr virus

Table 3: Logistic regression analysis to predict episodes of infection

Variable	Odds ratio (95% CI)	P-value
Day 10 (n=38)		
Neutrophil count (cell X 10 ⁹ /L)	274.55 (0.00 - 6.8 ⁹)	0.518
Lymphocyte count (cell X 10 ⁹ /L)	0.83 (0.01- 63.52)	0.934
QuantiFERON Monitor (per IU/ml)	0.96 (0.93 - 0.99)	0.022*
Engraftment (n=33)		
Neutrophil count (cell X 10 ⁹ /L)	0.93 (0.75-1.16)	0.523
Lymphocyte count (cell X 10 ⁹ /L)	0.76 (0.22-2.71)	0.677
QuantiFERON Monitor (per IU/ml)	1.00 (1.00-1.00)	0.726

* p<0.05 is considered statistically significant

Figure legends

Figure 1: IFN- γ levels (IU/ml) of the cohort over time post transplant (n=40).

B- baseline, PC- pre-conditioning, D10- day 10.

Figure 2: IFN- γ levels (IU/ml) over course of transplant stratified by recipient age (n=40).

Young <35 yrs, middle= 35-55 yrs, old >55 yrs.

B- baseline, PC- pre-conditioning, D10- day 10.

Figure 3A: IFN- γ levels stratified for patients who did and did not develop infection at a particular time point post transplant (n=200 time points).

Figure 3B: IFN- γ levels stratified for patients who did and did not develop a microbiologically-defined infection (MDI) at a particular time point post transplant.

Figure 4: Infective episodes by type of pathogen and days post transplant.

Figure 5: IFN- γ levels (IU/ml) in patients stratified for cytomegalovirus viral load (CMV VL) greater or less than 1000 copies per ml. (n=253 time points)(P=0.001)

Figure 6A: IFN- γ levels in patients stratified for status of acute GVHD (aGVHD): no aGVHD requiring treatment (89 timepoints), the blood draw “prior to aGVHD” requiring treatment (9 timepoints), and blood draws whilst “On aGVHD treatment” (6 timepoints). A total of 9 patients had aGVHD requiring treatment. Wilcoxon rank sum comparison of “prior to aGVHD” treatment to “on aGVHD treatment” (p=0.88)

Figure 6B: IFN- γ levels in patients stratified for status of chronic GVHD (cGVHD): “no cGVHD” requiring treatment (66 timepoints), the blood draw “prior to cGVHD” requiring treatment (10 timepoints), and blood draws whilst “On cGVHD treatment” (14 timepoints), using blood draws from day 90 onwards. A total of 11 patients had cGVHD requiring treatment. Kruskal-Wallis equality-of-populations rank test comparing the three groups (p=0.21).

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