Structured presurgery prehabilitation for aged patients undergoing elective surgery significantly improves surgical outcomes and reduces cost: A nonrandomized sequential comparative prospective cohort study

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Abstract

Background: With increasing global life expectancy, the number of major surgeries performed on aged adults invariably increases. This study aimed to examine the effectiveness of a structured prehabilitative program for aged colorectal cancer patients in improving short-term surgical outcomes.

Methods: A prospective philanthropically sponsored Programme for Enhanced Elderly Recovery at Sengkang General Hospital (PEERS) was initiated in February 2017 for patients \geq 70-years-old who were due to undergo elective colectomies. These patients were put through a 2- to 4-week-long program before surgery, which included geriatric assessment, nutrition supplementation, and resistance training. They were compared with patients from a similar age group before PEERS was introduced (non-PEERS).

Results: Fifty-eight patients, with a median age of 78.5 (70-93) years, were recruited from a single institution to undergo PEERS. Baseline characteristics between the groups were similar. There was no significant improvement of anthropometric and functional characteristics before and after PEERS. Duration of hospitalization was shorter in the PEERS group (9 vs 11 days, P = 0.01). Both groups had similar 30-days' morbidity rates (8.6% vs 17.4%, P = 0.26). The PEERS group had significant improvement in their median EuroQol-5 Dimension score (0.70 presurgery to 0.80 6-months' postsurgery, P = 0.01). After multivariate

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Conclusion: A standardized prehabilitation program for aged adults reduced the duration of hospitalization, improved the quality of life after surgery, and reduced costs.

KEYWORDS

aging, colorectal cancer, costs, prehabilitation, surgery, surgical outcomes

INTRODUCTION

The world is witnessing an unrelenting "silver tsunami." According to the World Health Organization, the global life expectancy has steeply risen by 8.4 years from 1990 to 72.6 years old in 2019, with countries like the United States of America surpassing 80 years old.¹ The aging population phenomenon is starting to put a strain on the economies and healthcare systems of several Asian countries like Japan and Korea.^{2,3} A fundamental feature of aging is the loss of muscle mass and strength, also termed as "sarcopenia."^{4,5} Sarcopenia has been defined based on consensus clinical definitions of the Asian Workgroup for Sarcopenia (AWGS) or European Workgroup for Sarcopenia (EWGS), incorporating skeletal muscle mass evaluation with functional components like grip strength and gait speed.⁶ Sarcopenia is inextricably linked with frailty, which has garnered increasing attention in literature.^{7,8}

Age is recognized as a nonmodifiable independent risk factor for poor surgical outcomes owing to the inevitable sequelae of sarcopenia, which decreases physical and functional reserves.^{9,10} In populations of older people, physiological reserves are further diminished with other comorbidities, such as ischemic heart disease or chronic kidney disease. This deficit in reserves not only predisposes aged patients to having an increased risk of surgical and anesthetic complications but also results in them taking a much longer time to recover from uncomplicated surgeries.^{11,12} This culminates in most aged patients requiring a longer hospitalization duration that inevitably leads to increased risks of nosocomial infections, further decreasing their chances of fully returning to baseline function despite rehabilitation efforts.¹³ All the above translates to a poorer quality of life (QoL) and an increase in healthcare costs.¹⁴

Enhanced recovery after surgery (ERAS) is a protocolized, evidence-based multimodal approach that has been demonstrated to get patients back to the community with less surgical morbidity.^{15,16} Most of these interventions center on immediate preoperative, intraoperative, and postoperative practices. In aged patients who have lower baseline reserves, the emphasis will be countering the effects of sarcopenia to improve their physical, physiological, and functional reserves, allowing them to take on the stress of surgery.^{17,18} Therefore, the concept of prehabilitation was conceived to achieve the abovementioned outcomes for patients who are due to undergo surgery.

Evidence around prehabilitation remains scarce. The details of a prehabilitation program, such as the regimens of nutrition and physical exercise are not firmly established.^{19,20} Uptake and compliance to a prehabilitation program, which potentially delays surgery, are also not well studied.^{20,21} There is also a lack of concrete evidence evaluating the benefits of the concept of prehabilitation for older age surgical patients. The primary aim of this study was to evaluate the impact of Programme for Enhanced Elderly Recovery at Sengkang General Hospital (PEERS) on the short-term surgical outcomes such as duration of hospitalization and 30-day morbidity and mortality. The secondary aim was to evaluate the effects of PEERS on physical and functional measures.

MATERIALS AND METHODS

Prehabilitation program

In the authors' institution, a philanthropically sponsored PEERS was initiated in February 2017 for patients 70 years old and older who were due to undergo major colectomies. This provided the opportunity for suitable patients in this vulnerable cohort to reap the benefits of a structured multidisciplinary prehabilitation program prior to surgery. Clinicians, including geriatricians, dietitians, and physiotherapists, could assess and intervene with physical and functional fall protection measures, nutrition supplementation, and resistance training exercises. These interventions also served to improve the patients' physical, physiological, and functional reserves in anticipation to their procedure. The interventions were as follows:

- 3 weeks of oral nutrition supplementation as recommended by the dietetics team,
- 3 weeks of resistance exercise using a resistance band with weekly review by the physiotherapies,

- one geriatrician consultation to optimize for polypharmacy and other "geriatric giants" (confusion, falls, incontinence, immobility, pressure injury), and
- one transthoracic echocardiogram and cardiovascular consult to evaluate and optimize cardiac risk for operation.

Another advantage of the program was the early evaluation of the patients' home situation. After surgery, care arrangements can be initiated and planned in advance to ensure the residence is equipped to receive the patient after surgery. The patients' home environments were pre-evaluated by the physiotherapist and/or geriatricians. Modification of the home environment, such as the installation of grip rails and antislip mats, can then be initiated early and be ready for the patient's eventual discharge from surgery.

Patient recruitment

After obtaining ethical approval from the institutional review board (SingHealth Centralised Institutional Review Board 201611-00064), we proceeded to conduct a prospective cohort study and recruited patients into the PEERS program. The study was conducted in compliance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies. Inclusion criteria for the program included the following characteristics:

- are 70 years of age and above,
- · have a diagnosis of resectable colorectal cancer,
- · are fit for elective surgery, and
- are able to mentally and physically adhere to the study protocol and attend dietitian and physiotherapy sessions (ie, patients who have dementia or schizophrenia diagnoses, patients who are restricted to their bed, and patients who are wheelchair users).

Exclusion criteria for the program included patients with tumor-related crises such as perforation, bleeding, and obstruction of the tumor or near-obstruction of tumors, which precluded patients from being in the program for 2–4 weeks.

Suitable patients were recruited into the program by the surgical team. Informed consent was obtained from these patients prior to enrollment. Upon enrollment, patients were assessed by the dietitian and physiotherapist. Baseline biochemical and clinical nutrition assessment, including anthropometric measurements and dynamic functional assessments, were performed upon enrollment. Anthropometric measurements included body weight, mid-arm circumference and tricep-fold thickness. Functional parameters included grip strength, gait speed, 30-s chair rise repetitions, functional reach, and the 6-min walk test. Frailty level of each patients was also assessed using the clinical frailty scale: a validated method examining the patient's frailty level in comparison with the ability to provide care for themselves (Supplementary Material Figure 1).²² A program coordinator kept track of the progress of the patients during the program, facilitating the patients' appointments and ensuring adherence.

Upon the completion of the program, patients were reassessed clinically prior to surgery ("After PEERS" in Table 3), evaluating their physical and functional changes before and after the program. Surgery was performed by a team of six consultant-grade surgeons. Perisurgical parameters were collected, including short-term surgical outcomes such as length of hospitalization after operation, disposition after discharge from the acute hospital setting, and 30-day mortality and morbidity. Surgical morbidity was classified according to the Clavien-Dindo Classification.²³

QoL assessment was also conducted using the validated EuroQol-5 Dimension (EQ-5D) questionnaire, which was administered prior to the PEERS, and at 1, 3, and 6 months postoperation. EQ-5D, first developed in Europe, is a validated preference-based generic health status QoL measurement tool evaluating five domains: mobility, self-care, usual activities, discomfort, and anxiety/depression. EQ-5D provides a utility score measuring from 0 (signifying death) to 1 (signifying perfect health).^{24,25}

To evaluate the true benefit of PEERS, a sequential comparison was performed with an earlier cohort of colorectal patients of a similar age who underwent colorectal resections and managed by the same group of surgeons predating the initialization of the PEERS program. These patients would have qualified for PEERS if the program was available then. Short-term surgical outcomes were compared between the groups to ascertain the impact of the program. Both groups of patients were managed based on ERAS principles adopted by the department. Both groups were followed up, and at the time of analysis, their last date seen by a medical professional, as captured on the electronic medical records, were recorded. Death occurred if it was reflected on the electronic medical records by the National Death Registry at the time of analysis.

Individual patient's financial details were unavailable for analysis due to prevailing laws pertaining to the use of personal financial data for research purposes. Cost savings were calculated based on the publicly available prevailing national average unsubsidized cost per day for a colonic resection in a public hospital.²⁶ This would have likely reflected the minimal cost difference between the groups.

Statistical analysis was performed using SPSS Version 25 (SPSS Inc, an IBM Company, Chicago, IL). Pearson chisquare test was used for the analysis of discrete variables,

TABLE 1 Patient demographics

Characteristics	PEERS	Non-PEERS	P-values
N	58	23	NA
Median age, years (range)	78.5 (70–93)	77 (70–90)	0.35
Male, n (%)	33 (56.9)	12 (52.2)	0.70
Recruitment weight, median (range), kg	56.9 (35.3-83.0)	59.3 (29.8–77.7)	0.88
Hemoglobin level, median (range), g/dl	11.2 (8.1–14.4)	11.3 (9.3–14.8)	0.64
Serum creatinine, median (range), μ mol/L	73 (30–263)	77 (22–135)	0.74
Serum albumin level, median (range), g/L	40 (25–51)	39 (18–46)	0.77
Ejection fraction, median (range), %	62 (30–76)	62.5 (58–75)	0.40
Location of tumor, n (%)			0.42
Colonic	43 (74.1)	19 (82.6)	
Rectal	15 (35.9)	4 (17.4)	

Abbreviations: NA, nonapplicable; PEERS, Programme for Enhanced Elderly Recovery at Sengkang General Hospital.

and Mann-Whitney *U* test or Kruskal-Wallis test was used to analyze continuous variables. A *P*-value of ≤ 0.05 was considered to be statistically significant. Multivariate analysis using multiple linear regression was performed for duration of hospitalization, controlling for possible confounders.

RESULTS

A total of 58 patients, with a median age of 78.5 (70–93) years, were recruited for PEERS program between February 2017 to March 2020. Just over half were male (n = 33, 56.9%), and a majority of the patients had colonic malignancy (n = 43, 74.1%). A majority of patients fell into the B grade in the clinical frailty scale (n = 42, 72.4%). In the preceding 1.5 years, from April 2016 to September 2018, 23 patients (with a median age of 77 [70–90) years) who were not recruited for PEERS were used for comparison. Univariate analysis revealed that all baseline characteristics were not significantly different in both groups, exhibiting similar baseline biochemical, demographic, and radiological information. Details are shown in Table 1.

In terms of the type of surgery received, there were significantly more laparoscopic procedures in the PEERS group compared with the non-PEERS group (62.1% vs 30.4%, P = 0.02). After histopathological assessment of the tumor, we found no significant difference in the individual National Comprehensive Cancer Network (NCCN) stage of disease. Details are shown in Table 2.

Effect on physical and functional parameters

The 58 patients who completed the PEERS program did not demonstrate a significant difference in anthropomet-

ric measurements (weight, mid-arm circumference, and triceps skinfold thickness) prior to ("Before PEERS" in Table 3) and after ("After PEERS" in Table 3) going through the nutrition and physical intervention prior to surgery. There was also no statistical difference in clinical nutrition assessment scores between the two time periods. In terms of dynamic functional measures, the most clinically significant improvement was seen in the 30-s chair rise repetition, with a median improvement of one repetition gained (-4 to 10, P = 0.06). The rest of the post-PEERS functional assessments (grip strength, gait speed, functional reach, and 6-min walk test) were similar to that of the pre-PEERS assessment. Details of the clinical nutrition assessment, anthropometric, and dynamic functional parameters can be found in Table 3.

Effect on surgical outcomes

Next, the effect of the PEERS program on the surgical short-term outcome was evaluated. In comparison with the non-PEERS group, the PEERS group demonstrated a significantly earlier median time to flatus (3 vs 4 days, P =0.02) and bowel movement (3 vs 4 days, P = 0.03), facilitating the return of bowel function after colorectal surgery. Next, both groups exhibited similar 30-day mortality (0% vs 0%, P = 1.00) and morbidity (41.3% vs 47.8%, P = 0.60) rates. The rate of serious morbidity, defined as Clavien-Dindo grade III and more, were also similar between both groups (8.6% vs 17.4%, P = 0.26). Median length of hospitalization was significantly shorter for the PEERS group in comparison with the non-PEERS group (9 vs 11 days, P =0.01). This translated to an estimated healthcare cost savings of up to USD\$3482. Details of the surgical outcomes are shown in Table 4.

After multivariate analysis using multiple linear regression, controlling for modality of surgery (laparoscopic/

TABLE 2 Surgical and histopathological characteristics

Characteristics	PEERS, N (%)	non-PEERS, N (%)	P-values
Ν	58	23	NA
Type of surgery			0.02
Open	21 (36.2)	16 (69.6)	
Laparoscopic	36 (62.1)	7 (30.4)	
Laparoscopic-converted-to-open	1 (1.7)	0	
T stage			0.92
T1	5 (8.6)	2 (8.7)	
T2	9 (15.5)	2 (8.7)	
T3	30 (51.7)	12 (52.2)	
T4	12 (20.7)	4 (17.4)	
Missing	2 (3.4)	3 (13.0)	
N stage			0.94
NO	34 (58.6)	13 (56.5)	
N1	9 (15.5)	3 (13.0)	
N2	13 (22.4)	4 (17.4)	
Missing	2 (3.4)	3 (13.0)	
M1	1 (1.7)	1 (4.3)	0.49

Bolded *P* values are statistically significant *P* values (P < 0.05).

Abbreviations: NA, nonapplicable; PEERS, Programme for Enhanced Elderly Recovery at Sengkang General Hospital.

TABLE 3 Changes after PEERS intervention

Characteristics	Before PEERS	After PEERS	Changes	P-values
Median weight, kg (range)	56.9 (35.3-83.0)	56.5 (38.0-83.9)	0 (-4.5 to 3.4)	0.91
Median mid-arm circumference, cm (range)	23.9 (18.2–39.0)	23.7 (18.6–36.8)	0 (-9.0 to 4.1)	0.85
Triceps skinfold thickness, median (range), mm	14 (6–30)	13 (7–28)	0 (-13 to 10)	0.60
SGA score, median (%)			NA	0.24
4	2 (3.4)	3 (5.2)		
5	18 (31.0)	16 (27.6)		
6	26 (44.8)	21 (36.2)		
7	11 (19.0)	13 (22.4)		
Unknown	1 (1.7)	7 (12.1)		
Grip strength, median (range), kg	20.2 (7.5–35.0)	20.5 (9.0-35.9)	0.7 (-7.0 to 7.9)	0.61
Gait speed, median (range), m/s	0.84 (0.11-1.56)	0.94 (0.12–1.78)	0.09 (-1.31 to 0.60)	0.32
30-s chair rise, median (range), repititions	11 (4–26)	12 (3–28)	1 (-4 to 10)	0.06
Functional reach, median (range), cm	20 (7.0–38)	22.4 (7.0-43.5)	2 (-14 to 13.86)	0.47
6-min walk test, median (range), m	312.0 (35.0-600.0)	330.1 (40.0–687.0)	11.0 (-240.0 to 184.0)	0.52

Abbreviations: NA, nonapplicable; PEERS, Programme for Enhanced Elderly Recovery at Sengkang General Hospital; reps, repetitions; SGA, Subjective Global Assessment.

open) and 30-day morbidity, the PEERS groups had, on average, 6.8-day-shorter duration of stay in hospital (CI, 1.2–12.4; P = 0.018). This translates to an estimated health-care cost savings of up to USD\$11,838.80.

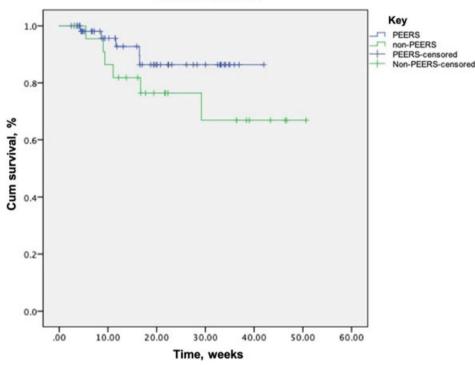
Median follow-up duration for the PEERS group was 16.2 (range: 2.5–42.0) months and 21.6 (range: 3.0–50.7) months for the non-PEERS group. The mean survival of

PEERS and non-PEERS patients are 37.9 (SD: 34.6–41.2) months and 39.1 (SD: 31.2–46.9) months, respectively. The Kaplan-Meier curve for 2-year overall survival of both study cohorts is illustrated in Figure 1. Even though both survival curves seemed to diverge at 10 months, favoring the PEERS group, there was no statistical significance based on the log-rank test (P = 0.17).

Characteristics	PEERS	Non-PEERS	P-values
Median time to flatus, days (range)	3 (1-7)	4 (1–7)	0.02
Median time to bowel movement, days (range)	3 (1–7)	4 (1–7)	0.03
Median length of hospitalization, days (range)	9 (4–32)	11 (5–84)	0.01
Discharge disposition, n (%)			0.69
Home	48 (82.8)	20 (87.0)	
Rehabilitation facility	7 (12.1)	2 (8.7)	
Nursing home	1 (1.7)	1 (4.5)	
Unknown	2 (3.4)	NA	
30-day mortality, n (%)	0 (0.0)	0 (0.0)	1.00
30-day morbidity, n (%)	24 (41.3)	11 (47.8)	0.60
Clavien-Dindo III	3 (5.2)	3 (13.0)	0.22
Clavien-Dindo IV	2 (3.4)	1 (4.5)	0.85

Bolded P values means they are statistically significant (P < 0.05).

Abbreviations: NA, nonapplicable; PEERS, Programme for Enhanced Elderly Recovery at Sengkang General Hospital.



Survival functions

FIGURE 1 Survival curves for PEERS vs non-PEERS patients; PEERS, Programme for Enhanced Elderly Recovery at Sengkang General Hospital

Effects on QoL

Patients recruited for PEERS started with a median EQ-5D score of 0.70 (range: 0.30–1.00). Follow-up assessments at each evaluation interval demonstrated an increasing trend, which significantly improved at 6-months postsurgery with a score of 0.80 (P = 0.001, range: 0.50–1.00). Details are shown in Table 5.

DISCUSSION

The concept of prehabilitation focuses on the replenishment of diminished physical and functional reserves to assist the patient to overcome a planned physiologically stressful event, in our setting, a major surgery.^{14,27} The results from this study demonstrate that although the physical and functional attributes did not reach

TABLE 5 Quality of life assessment using EuroQol-5 Dimension Health Questionnaire

Value	Prior to PEERS	1-month postoperation	3-months postoperation	6-months postoperation	P-value
Median score (range)	0.70 (0.30-1.00)	0.78 (0.25–1.00)	0.80 (0.20-1.00)	0.80 (0.50-1.00)	0.001

Bolded P values means they are statistically significant (P < 0.05).

Abbreviation: PEERS; Programme for Enhanced Elderly Recovery at Sengkang General Hospital.

statistically significant improvements, there was a significant improvement in short-term surgical outcomes, including time to return to bowel function and duration of hospitalization. These results suggest that physiological reserves may have improved after prehabilitation, resulting in better surgical outcomes. A relative short duration of intervention is the most plausible explanation accounting for no differences observed in both groups with regards to the measurable physical and functional attributes prior to surgery, yet patients still enjoyed the benefit from improved physiological reserves. This may represent that monitoring of physical or functional improvement may not be such an accurate measure of the improvement in physiological reserves from prehabilitation. Next, several studies have reported a twofold increase in surgical morbidity and mortality with frailty associated with age.²⁷ Even though the PEERS group trended towards a lower 30-day morbidity rate (8.6% vs 17.4%), it did not reach statistical significance (P = 0.26). We acknowledged that the small sample size of ours may have masked the effects of prehabilitation on surgical morbidity and mortality. Although there may be no statistical difference in morbidity between the groups, the duration of hospitalization was still significantly shorter (P = 0.018), this possibly was a result of patients reaching a physical and functional status adequate enough to be discharged quicker in the PEERS group.

In addition to the improved surgical outcomes, there was a progressive and significant improvement in generic health QoL scores in the months after surgery. This demonstrated the key role prehabilitation had on the functional and psychological outcomes for this traditionally vulnerable group of patients who have a significant risk of deconditioning, which impacts their QoL. The risk of compromising QoL often dissuades clinicians and patients from opting for major surgery. Hence, patient's enrollment into a structured multidisciplinary approach to prehabilitation, which integrates clinical, nutrition, and physical interventions,^{28,29} can further reassure patients, clinicians, and their families that the outcomes after surgery may be improved.

Healthcare cost have been exponentially increasing globally.^{30,31} With the reduction of surgical complications and a shorter length of stay, these further translate to cost savings for the industry. Our study reported an average of USD\$11,838.80 per patient just based on the reduction

in duration of hospitalization. This cost was calculated based on estimates from a public healthcare system, which is considerably less than an insurance-based healthcare system. The cost-saving estimations also do not factor in potential savings from a reduction in complications and hence may be a conservative estimate. A prehabilitation programme does appear promising in terms of cost savings and may retard the upward spiral of healthcare costs. Such a preemptive intervention prior to surgery may potentially place less financial strain on the patients, their families as well as the healthcare system, especially as this group of patients tend to be beyond their economically independent years.

Nutrition supplementation and resistance training have both been recognized as the cornerstones in the treatment or retardation of sarcopenia.³² Sarcopenia is unfortunately part of the natural aging process. The loss in muscle bulk and strength have both negative effects on function and rehabilitation after surgery.³³ Thus, the intent of PEERS was to improve the quality of muscles, minimize the effects of sarcopenia with the eventual aim to improve surgical outcomes. The study achieved these desired outcomes with shorter hospital stay and improved QoL outcomes, despite the sample size limitations. It has laid the groundwork for further validation studies with a larger study sample or in the setting of a randomized controlled trial.

The increased usage of laparoscopic surgery in the PEERS group could have confounded surgical outcomes like time to return of bowel function and length of hospitalization. The decision for open or laparoscopic surgery was determined by the primary surgeon. The reason for this could be due to significant emerging evidence in literature to suggest it is as safe to perform laparoscopic surgeries in the aged adults between the two time periods, which played a part in the increased use of laparoscopy in the PEERS group.34-36 The low conversion rate of 1.7% further verified that these older patients could tolerate the demands of laparoscopy after a period of prehabilitation. The team acknowledged this and thus performed the multivariate analysis of our data particularly focused to tackle this difference between the groups and found that when the modality of surgery is factored in, the differences in average duration of hospitalization was maintained.

There were several limitations in our study that need to be acknowledged. First, the small sample size may have masked the effects of prehabilitation on physical and functional attributes as well as morbidity outcomes. Next, the use of a retrospective cohort could have potentially lead to selection and recall bias. Despite so, the trends observed from this study revealed the benefits of a prehabilitation program and has laid the groundwork for future studies. Another limitation of this study is that there was no molecular or Dual Energy X-Ray (DEXA) assessment of the muscle tissue preintervention and postintervention. This might help elucidate the effects of nutrition and resistance exercise on muscle quality. By identifying the regulatory mechanisms of sarcopenia modified by the PEERS' intervention, we might be able to further draw causal links between the intervention and outcomes. This would assist to further optimize the program in the future.

CONCLUSION

With a standardized prehabilitation program for older patients before elective colorectal resections, the duration of hospitalization could be reduced with improvement in QoL outcomes. These may translate to reduction in healthcare costs for older patients undergoing colorectal surgery.

CONFLICT OF INTEREST None declared.

FINANCIAL DISCLOSURE

Altruistic anonymous donor funded the PEERS program.

AUTHOR CONTRIBUTIONS

Min-Hoe Chew, Fung-Joon Foo, and Winson J. Tan contributed to the conceptualisation and the design of the research; Frederick H. Koh, Jason M.W. Chua, Shawn S.X. Kok, Dulcena Yen, and Caroline H. Loh contributed to the acquisition and analysis of the data; Frederick H. Koh, Sharmini S. Sivarajah, and Leonard M.L. Ho contributed to the interpretation of the data; and Frederick H. Koh drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Due to institutional restrictions, raw data would not be published but can be requested from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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