

Insisting on Life Dignity: Advance Care Planning in Taiwan During COVID-19 Pandemic

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Abstract

Background:

The coronavirus disease 2019 (COVID-19) outbreak is a global public health crisis that has affected the implementation of advance care planning (ACP) in Taiwan. The purpose of this study is to (1) confirm that COVID-19 significantly reduced public participation in ACP, (2) identify factors influencing the implementation of ACP during the COVID-19 pandemic and how they differ from those before the COVID-19 outbreak.

Methods:

An observational study from retrospective review of medical chart and clinical information. This is a hospital-based study to examine the characteristics of ACP implementation in Taiwan during COVID-19. A total of 1,253 participants were recruited, including 916 people who had completed ACP from September through December 2019, and 337 people from January through April 2020.

Results:

This study representing an approximately 65% decrease in ACP participation after COVID-19 outbreak. The cancellation rate of ACP during COVID-19 is higher before outbreak. After COVID-19 outbreak, Participation rate of disadvantaged populations increased from 16.92% to 21.66%. The percentage of participants with caregiver experiences decreased from 31.66% to 23.44%. Participants who did not wish for their families to bear decision-making responsibilities increased from 44.00% to 52.52%. The percentage of offspring participation increased from 86.57% to 90.80%. The percentage of individuals completing ACP after the outbreak without signing an advance directive increased from 5.57% to 9.20%. The COVID-19 pandemic significantly reduced participation in ACP.

Conclusions:

This study directly compared the ACP implementation before and after COVID-19, which is a tremendous global health crisis influencing the conceptions of life and death. COVID-19 has threatened the public's health and has changed ACP in the healthcare system by increasing public awareness of the topic of death. After COVID-19, both medical staff and the public should clearly express their opinions on terminal care. Policy supports and active participation of medical team can encourage disadvantages to complete ACP. Healthcare workers should provide palliative and terminal care services in which patient comfort and dignity are the primary focus of care.

Trial registration:

This study was approved on 3 June 2020 by the Taipei City Hospital Institutional Review Board (Case No.: TCHIRB-10808008-E).

Introduction

The COVID-19 pandemic has been an ongoing public disaster since 2019. The virus has spread at an unprecedented speed worldwide and has developed into the largest epidemic in modern times.[1] Due to the characteristics of the virus, the future epidemic situation is full of variables, and its impact on society is very extensive, including public life safety, social and psychological problems etc. In addition, for clinicians, everyone needs to change the way of thinking in the past and re-examine working methods to deal with the problems caused by the public health crisis.[2]

Advance care planning (ACP) significantly improves patient and family satisfaction and well-being. Consistency between care preferences and service provision[3]also reduces the decision-making burden on family members as well as their stress, depression, survivor's grief, and posttraumatic stress.[4] Several countries have also passed legislation to encourage and promote ACP; however, there is still a big gap between the high recommendations of ACP and the low completion rate of AD, which shows that the implementation of ACP is still hindered by many factors. For instance, patients and doctors are unwilling to initiate ACP discussions, discuss the cultural taboos of death, doctors' lack of time and communication skills, cannot implement patients' advance care plan due to the doctor's personal values, and patient's unrealistic expectations toward the efficacy of medical treatment.[5–7]

There are many determinants that affect people's advance care planning, including demographic characteristics, health status, knowledge and attitudes regarding advance directives, and cultural values and beliefs.[8] Levi[9] demonstrated that self-concern, including autonomy, dignity, meaningful existence, quality of life, possible treatment outcomes, and the burden and suffering of psychological and physical burdens of life-prolonging medical interventions, have the largest impact on ACP participation. David et al.[10] also indicated that the more actively patients manage their overall personal health care, the higher their ACP participation is. Nouri et al.[11] Demonstrated that health literacy moderates health-related knowledge. By increasing the knowledge of ACP and developing easy-to-read materials, people with low health literacy can improve their understanding of ACP, thereby increasing the completion rate of advance decisions. In general, economic disadvantages, limited access to ACP or misunderstanding of relevant information may prevent disadvantaged groups from completing ACP.[12] Cultural values such as religious beliefs, trust in the healthcare system, the comfort of patients and physicians in discussing death, and patients' attitudes toward decision-making, all affect patients' acceptance of ACP.[13]

Since the Patient Right to Autonomy Act was formally promulgated in Taiwan on January 6, 2019, the participation of ACP has increased significantly, and 11,266 people completed ACP that year. The Act stipulates that declarants receive consultation services provided by the medical institution regarding ACP and have their advance directive affixed with the institution's seal. In practice, hospitals and medical institutions establish ACP clinics for the public to consult with a medical team to discuss participants' preferences and decisions of medical care in specific five clinical conditions before completing AD. After the outbreak of COVID-19, concerned authorities called upon the public to reduce hospital visits, and

medical institutions proposed policies restricting visits to reduce the number of hospital visitors. These restrictions might have affected people's willingness to visit hospitals and implement ACP.

However, Curtis[14] emphasized the importance of ACP during the COVID-19 pandemic and the ethical challenges that infectious diseases pose to the healthcare systems of many countries. This proposal has been supported by many international scholars. In Canada, Jorsvik et al. developed the Advance Care Planning During COVID-19 Toolkit to stress the importance of ACP during the COVID-19 pandemic.[15] Work teams in the United States also provided ACP tools and instant message to medical personnel. For instance, the Respecting Choices provides online ACP workshops to encourage open dialogue among medical staff.[16] The COVID-Ready Communication Playbook authored by VitalTalk provides clinicians with coping strategy when facing a global health crisis.[17] The National Institute for Health and Care Excellence also developed the COVID-19 Rapid Guideline[18] to ensure the safety of critically ill patients and medical staff. The guidelines even suggest that in addition to actively treating covid-19 patients, medical staff should also initiate ACP discussions.[19]

This study thus analyzes and compares the status of ACP implementation before and after the outbreak of COVID-19 in Taiwan as well as potential influencing factors. The purpose of this study is to (1) confirm that COVID-19 significantly reduced public participation in ACP, (2) identify factors (e.g., demographic characteristics, motivation to complete ACP, health status, caregiver experience, ACP implementation method, and medical decision content) influencing the implementation of ACP during the COVID-19 pandemic and how they differ from those before the COVID-19 outbreak.

Methods

Participants

Individuals who completed ACP at regional hospitals in Northern Taiwan were selected as participants, and data from September to December 2019 and from January to April 2020 were collected. Inclusion criteria were individuals who (1) voluntarily visited the hospital for ACP services, (2) were aged 20 years or older, and (3) were not under the declaration of guardianship. ACP was performed in one of the following settings: outpatient clinics, ACP at home, ACP at care facilities. Among all participants, from September 2019 to December 2019, 916 people participated in ACP, and from January 2020 to April 2020 during the outbreak of COVID-19, 337 people participated in ACP.

The demographic data of participants were collected from the hospital's registration data, including gender, age, social welfare status. (Table 1) This study was approved by the Taipei City Hospital Institutional Review Board (Case No.: TCHIRB-10808008-E). The datasets generated and analysed during the current study are not publicly available due to privacy of patient information, but are available from the corresponding author on reasonable request.

Table 1
Demographic Information of Participants

Variable	Advance Care Planning Implementation Period	
	108/9-108/12 (N = 916)	109/1-109/4 (N = 337)
Sex		
male	312(34.06%)	117 (34.72%)
female	604(65.94%)	220(65.28%)
Age		
20 ~ 29years	25 (2.73%)	8(2.37%)
30 ~ 39years	68(7.42%)	30(8.90%)
40 ~ 49years	94(10.26%)	43(12.76%)
50 ~ 59years	195(21.29%)	76(22.55%)
60 ~ 69years	298(32.53%)	88(26.11%)
70 ~ 79years	170(18.56%)	65(19.29%)
80 ~ 89years	57(6.22%)	22(6.53%)
90 years above	9(0.98%)	5(1.48%)
Social welfare status (multiple choices)		
None	761(83.08%)	264(78.34%)
Low- and middle-income Households	20(2.18%)	7(2.08%)
People with disabilities	93(10.15%)	43(12.76%)
People with serious illnesses	42(4.59%)	24(7.12%)
CDR > 0.5	3(0.33%)	5(1.48%)
Older adults living alone	15(1.64%)	7(2.08%)
Homeless people	1(0.11%)	2(0.59%)
N: Number of participants; CDR: Clinical Dementia Rating		

Data Analysis

This study performed a retrospective secondary data analysis. The data collected from written documents completed by the participants after implementing ACP, including advance decision, advance care planning consultation record and end-of-life care preferences consultation record. Descriptive

statistics (frequencies and percentages) and a chi-square test were used to analyze the differences in demographic characteristics, perform settings of ACP, motivation for ACP, and decisions on medical care between participants during the two periods.

Results

Associations among demographical variables and periods of ACP implementation (Table 2)

Table 2
Associations among demographical variables and periods of ACP implementation

Variable	Advance Care Planning Implementation Period		
	108/9-108/12 (N = 916)	109/1-109/4 (N = 337)	Chi-Square
Sex			
Male	312(34.06%)	117 (34.72%)	.47(.828)
Female	604(65.94%)	220(65.28%)	
Age			
65years	542(59.17%)	199(59.05%)	.001 (.969)
> 65years	374(40.83%)	138(40.95%)	
Social welfare status			
None	761(83.08%)	264(78.34%)	3.716(.054)
Disadvantaged populations*	155(16.92%)	73(21.66)	
Health status (self-report)			
Without diseases	606(66.16%)	196(58.16%)	6.839(.009*)
With diseases	310(33.84%)	141(41.84%)	
Caregivers' experiences			
No	504(55.02%)	209(62.02%)	4.331(.037*)
Yes	402(43.89%)	127(37.69%)	
Relationship with ACP participant			
Spouse	48(5.24%)	27(8.01%)	3.238(.072)
Parent	290(31.66%)	79(23.44%)	8.474(.004*)
Adult children	8(0.87%)	3(0.89%)	.972(.324)
Sibling	13(1.42%)	7(2.08%)	.645(.333)
Other	42(4.59%)	12(3.56%)	.321(.571)
N: Number of participants; ACP: Advanced Care Planning; *disadvantaged populations (including low- and middle-income households, people with disabilities, people with serious illnesses, those with a clinical dementia rating of 0.5 or higher, older adults living alone, and homeless people)			

Three-hundred and thirty-seven people completed ACP from January through April 2020, representing an approximately 65% decrease in ACP participation compared with those (916 individuals) who completed

ACP from September through December 2019. In fact, the cancellation rate of ACP during COVID-19 is also significantly higher than the period before outbreak (September – December 2019: 3%; January – April 2020: 20%). Participants from the two periods exhibited no significant differences in sex or age. After the COVID-19 outbreak, the ACP participation rate of disadvantaged populations (e.g., low- and middle-income individuals, people with disabilities, patients with serious illness or injury, those with a clinical dementia rating (CDR) of 0.5 or higher, older adults living alone, and homeless people) increased from 16.92–21.66%. Compared with the general public, the ACP participation rate of the disadvantaged population increased more during the pandemic; however, the difference was not significant.

According to participants' self-reports, the number of participants without illness before and after the COVID-19 outbreak was 66.16% and 58.16%, respectively; the proportion of healthy ACP participants decreased significantly during the COVID-19 pandemic. The percentage of participants with caregiver experience was 43.89% and 37.69% before and after the COVID-19 outbreak, respectively; the proportion of ACP participants with caregiver experience decreased significantly during the COVID-19 pandemic. The percentage of participants with experience caring for parents was 31.66% before the outbreak of COVID-19, but the percentage decreased significantly to 23.44% after the outbreak.

Associations among implementation methods, motivation for ACP and periods of ACP (Table 3)

Table 3
Associations among implementation methods, motivation for ACP and periods of ACP

Variable	Advance Care Planning Implementation Period		
	108/9-108/12 (N = 916)	109/1-109/4 (N = 337)	Chi-Square
Perform settings of ACP			
Outpatient clinics	756(82.53%)	273(81.01%)	.390(.532)
Inpatient clinics	16(1.75%)	6(1.78%)	.002(.968)
ACP completed at home	12(1.31%)	12(3.56%)	6.643(.010*)
ACP completed at care facilities	19(2.07%)	0(0.00%)	7.098(.008)
Group Visits for ACP	113(12.34%)	46(13.65%)	.384(.536)
Motivation for ACP (multiple choices)			
Participant suffering from diseases	66(7.42%)	26(7.42%)	.126(.723)
Being single	86(9.39%)	27(8.01%)	.496(.481)
Pursuing dignity and respect in end-of-life care	620(67.69%)	218(64.69%)	.596(.440)
Prearrangement for life decisions	552(60.26%)	186(55.19%)	2.045(.153)
Media reports	53(5.79%)	22(6.53%)	.285(.593)
Suffering from illness in family members	128(13.97%)	36(10.68%)	2.166(.141)
Not burden on families with decision-making	403(44.00%)	177(52.52%)	8.143(.004*)
Not become the burden of family	356(38.86%)	139(41.25%)	.815(.367)
Other	28(3.06%)	7(2.08%)	.823(.364)
N: Number of participants; ACP: Advanced Care Planning			

ACP was mainly performed in outpatient clinics before and after the COVID-19 outbreak (more than 80% in both periods). The percentage of ACP completed at home increased from 1.31% before the outbreak to 3.56% after the outbreak, which was significant. Participants who engaged in ACP during the pandemic were mostly motivated by the pursuit of a dignified life and end-of-life arrangements. However, the number of ACP participants driven by these two motivations declined compared to before the COVID-19 outbreak. ACP participants who did not wish to burden their families with decision-making responsibilities increased after the COVID-19 outbreak. Specifically, the percentage of ACP participants who did not wish for their families to bear decision-making responsibilities increased from 44.00–52.52%, which was a significant increase from before the COVID-19 outbreak.

Associations among the degree of kinship, health care agents and periods of ACP (Table 4)

Table 4
Associations among the degree of kinship, health care agents and periods of ACP

Variable	Advance Care Planning Implementation Period		
	108/9-108/12 (N = 916)	109/1-109/4 (N = 337)	Chi-Square
Designated HCA (multiple choices)			
No	848(92.58%)	312(92.58%)	.000(.998)
Yes	68(7.42%)	25(7.42%)	
Relationship with ACP participation (multiple choices)			
Spouse	17(1.86%)	5(1.48%)	.198(.656)
Adult child	18(1.97%)	16(4.75%)	7.227(.007*)
Sibling	15(1.64%)	3(0.89%)	.972(.324)
Friend	10(1.09%)	2(0.59%)	.645(.333)
Other	5(0.55%)	1(0.30%)	.321(.571)
Accompanied by first- or second-degree relatives (multiple choices)			
No	123(13.43%)	31(9.20%)	4.088(.043*)
Yes	793 (86.57%)	306(90.80%)	
Relationship with ACP participation			
Spouse	339(37.01%)	131(38.87%)	.365(546)
Adult child	135(14.74%)	62(18.40%)	2.490(.115)
Sibling	195(21.29%)	97(28.78%)	7.743(.005*)
Friend	248(27.07%)	89(26.41%)	.0555(.814)
Other	70(7.64%)	31(9.20%)	.806(.369)

The COVID-19 outbreak did not affect the appointment of health care agents (HCA), but after the COVID-19 outbreak, the percentage of participants designating their children as health care agents increased significantly. Regarding changes in the declarants' accompanying relatives from before to after the outbreak of COVID-19, the proportion of relatives within the second-degree of kinship increased from 86.57–90.80%; of these relatives, the percentage of offspring participation increased significantly.

Completion of advance decisions and decisions on medical care (Table 5)

Table 5
Completion of advance decisions and decisions on medical care

Variable	Advance Care Planning Implementation Period		Chi-Square
	108/9-108/12 (N = 916)	109/1-109/4 (N = 337)	
Complete documents of AD immediately after ACP			
Yes	865(94.43%)	306(90.80%)	5.311(.021*)
No	51(5.57%)	31(9.20%)	
Do not make decisions in 5 major clinical conditions			
Patient is terminally ill			
Life-sustaining treatment	53(5.79%)	33(9.79%)	6.186(.013*)
Artificial nutrition and hydration	53(5.79%)	33(9.79%)	6.186(.013*)
Patient is in an irreversible coma			
Life-sustaining treatment	52(5.68%)	33(9.79%)	6.598(.010*)
Artificial nutrition and hydration	52(5.68%)	33(9.79%)	6.598(.010*)
Patient is in permanent vegetative state			
Life-sustaining treatment	52(5.68%)	33(9.79%)	6.598(.010*)
Artificial nutrition and hydration	52(5.68%)	33(9.79%)	6.598(.010*)
Patient is suffering from severe dementia			
Life-sustaining treatment	52(5.68%)	33(9.79%)	6.598(.010*)
Artificial nutrition and hydration	52(5.68%)	33(9.79%)	6.598(.010*)
Other disease conditions announced by the central competent authority			
Life-sustaining treatment	54(5.90%)	32(9.50%)	4.996(.025*)
Artificial nutrition and hydration	54(5.90%)	32(9.50%)	6.996(.025*)

Percentage of participants who implemented ACP without completing advance decisions increased from 5.57% before the outbreak of COVID-19 to 9.20% after the outbreak. Similarly, the percentage of participants who did not make clinical decisions (e.g., life-sustaining treatment or artificial nutrition and hydration) for five major clinical conditions increased significantly after the outbreak of COVID-19.

Disussion

This study compared the implementation of ACP before the COVID-19 outbreak from September 2019 to December 2019 and after the COVID-19 outbreak from January 2020 to April 2020. During these two periods, the relevant hospital facilities and environment, ACP subsidy policies and the maturity of the medical team's execution skills were relatively consistent, thus minimizing the impact of factors unrelated to the pandemic.

Overall, the number of people participating in ACP decreased significantly after the COVID-19 outbreak. At the beginning of 2019, an average of 180 to 200 people implemented ACP every month. However, from January 2020 to April 2020, after the COVID-19 outbreak, the number of hospital visits and telephone consultations was greatly reduced, resulting in a 63% reduction in the proportion of ACP. Most of those who canceled the appointment expressed their hope to implement ACP after the pandemic ended, which shows that the COVID-19 epidemic has significantly reduced public participation in ACP.

However, a careful analysis of the demographic information of the participants showed that during the COVID-19 period, the percentage of illnesses increased significantly, and the proportion of disadvantaged groups increased from 16.92–21.66%. Elderly people with severe diseases or multiple diseases usually need ACP more than healthy people, but the taboo against discussing death in Chinese culture[20] and high death anxiety hinders the discussion of ACP among the elderly and patients with severe diseases. [21] This study shows that in response to the pandemic, the medical team adjusted the ACP implementation strategy. For patients who have urgent needs to discuss ACP but lack initiative (for example, patients with severe illness or mobility impairments receiving home-based medical care), medical staff actively initiate discussions about ACP, which greatly increases the number of ACP participants with diseases proportion. This finding resonates that most people expect to receive ACP information from their own doctors and believe that ACP activation is the responsibility of the healthcare provider.[22, 23]

During the COVID-19 pandemic, compared with the general public, the proportion of disadvantaged groups participating in ACP has increased; this was possibly due to the ACP subsidies and outreach to the disadvantaged population in need of ACP. Despite the overall decline in ACP participation during the pandemic, ACP participation among particular populations—who used to lack access to ACP—increased compared with that of the general public. With public policy and legislative support, the completion rate of advance directives in the United States increased from 16% in 1990 to 35% in 2013. Moreover, in late 2015, the Centers for Medicare and Medicaid Services (CMS) allows Medicare to pay for providing ACP consultation and the coverage of ACP consultation has extended from those with terminal illness to older adults. This Medicare benefit help to ensure that all older adults have the opportunity to discuss ACP, regardless of their economic or personal resources, which increased opportunities for all older adults to participate in ACP.[5] This study, along with the aforementioned examples, confirmed the importance of policy-based support and active participation of medical teams in implementation of ACP.

The results of this study on the implementation of ACP show that the proportion of ACP completed at home has increased from 1.31–3.56%. Although the proportion of participants is not much of the total, the growth rate has increased significantly. In the past, ACP was mainly performed in emergency departments, outpatient clinics, and general community settings. Few studies have focused on ACP for patients receiving domiciliary care, such as patients with chronic cardiovascular and pulmonary diseases. [24] In the present study and clinical observation show that medical teams significantly increased ACP accessibility during the pandemic by actively providing ACP to patients with severe illness or mobility impairments.

This study shows that during the COVID-19 pandemic, none of the residents living in nursing facilities participated in the ACP. This is very different from other countries that promote ACP during COVID-19, encouraging staff to proactively provide ACP discussion or review completed advance directives.[25] A possible reason for this discrepancy is that during the epidemic occur in Taiwan, facility staffs are required to comply with strict access policy to reduce infection. Such restrictions on the entry of medical personnel who provide the discussion of ACP into care facilities might have contributed to the ACP completion rate of 0 among facility residents in this study.

During the pandemic, the number of ACP participants with caregiver experience decreased significantly, and the percentage of ACP participants caring for their parents also decreased significantly. According to previous studies, those who take care of their loved ones and make medical decisions for their loved ones are involved in the end-of-life care of patients and have experienced the emotional and physical burden of supporting the frail and dying patients, making caregivers more likely than ordinary people to think about what they want in the future and motivating them to implement ACP.[9, 26] However, the study reported that the proportion of ACP participants with caregiver experience decreased significantly during the pandemic compared to participants without caregiver experience. This may be due to the same reason for canceling ACP appointments during the pandemic—caregivers worried about being infected and spreading to vulnerable care recipients. Therefore, despite the importance of ACP, they avoided going out and contacting medical personnel, which delayed the implementation of ACP.

Regardless of the impact of the pandemic, this study shows that the majority of ACP participants were motivated by pursuing a dignified life and end-of-life prearrangements. Levi[9] investigated the factors that influence individuals to engage in ACP found concern for self as the strongest influence for engaging in ACP which comprised valued being in control of their major life decision, the desire to maintain a meaningful existence, the ability to enjoy everyday life as well as the likely outcome related to physical, mental, and financial burden caused by life-sustaining treatments.

In addition to achieving a good death according to their own wishes, reducing the burden of decision-making on the family is also the main motivation for the declarant to complete the advance directive. [9, 20] Therefore, in ACP consultation, it is important to help individuals recognize and reflect on the impact of their end-of-life care decision on family and friends.[9] Although not wanting family members to take responsibility for decision-making is still the third motivation of ACP after the COVID-19 outbreak,

the proportion of choosing this motivation has increased significantly. This implied that in the face of unpredictable pandemic threats, participants are aware of the difficulty and torture of making quick medical decisions for others without understanding the values, thoughts or wishes of others. This awareness encourages individuals to complete advance decision, thereby reducing the burden of decision-making on family members.

After the COVID-19 outbreak, the ACP participation of first- and second-degree relatives, as well as the percentage of offspring participating and serving as health care agents increased significantly. According to The Patient Right to Autonomy Act, at least one relative of first or second degree of affinity shall accompany to attend ACP. Engaging in consultations enables patients to fully communicate with all parties (professionals and family members) before making their own decision.[27] Understanding the values and wishes among family members can promote family harmony. In traditional Chinese culture, family interaction still affects the doctor-patient relationship. Affected by family relationships, family ethics, filial piety, and family traditions, patients with autonomous decision-making capacity still expect their family members to participate in ACP.[28]

The percentage of offspring participating and serving as health care agents increased significantly during the pandemic. This increase was possibly due to relatively flexible working hours among the participants' offspring. Therefore, participants mainly selected their offspring as their companions for ACP consultations and appointed them as health care agents. By involving offspring in medical decision-making, a declarant can reduce conflicts between family members on medical decisions and the responsibility of offspring.

In addition to ACP participation among first- and second-degree relatives, the proportion of participants who did not complete AD or make clinical decisions on the five major clinical conditions immediately after ACP consultation increased significantly during the pandemic. According to clinical experiences, the phenomenon may be attributable to last-minute decisions made by relatives to participate in their own ACP discussion. For those individuals who originally served as the first- or second-degree relative of a declarant are more likely to participate in ACP and stimulate further consideration of their own value and preferences while perceiving the benefit in the process of ACP. However, it may take more time to decide what kind of care they want and then complete the official documents.

Conclusion

The global spread of COVID-19 has threatened the public's health and has changed the implementation of ACP. Policy supports and medical team's adjusted ACP implementation strategies can encourage disadvantages to complete ACP. In the post-COVID-19 period, which the epidemic situation may become more and more severe, actively initiated discussions on ACP between medical staff and the public is urgent and necessary.

Declarations

Ethics approval and consent to participate

1. This is a retrospective study. All methods were carried out in accordance with relevant guidelines and regulations. The research protocol have submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins.
2. Although the informed consent in this study was waived, this research protocol was approved on 3 June 2020 by the Taipei City Hospital Institutional Review Board (Case No.: TCHIRB-10808008-E).

Consent for publication

Not required.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to privacy of patient information, but are available from the corresponding author on reasonable request.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' contributions

The contribution each author made to the manuscript was below:

- 1.Chun-Yi Yang–Conception or Design of the work, Data analysis and interpretation, Rafting the article
- 2.Ching-Nu Liu–Conception or Design of the work, Data analysis and interpretation, Rafting the article
- 3.Chi-Cheng Yang–Critical revision of the article, Data analysis and interpretation
- 4.Zong-Dar Tsai–Data analysis and interpretation
- 5.Su-Fei Lin– Data collection
- 6.Hsin-Yi Lin– Data collection
- 7.Yen-Rong Huang– Data collection
- 8.Fu-Min Sun– Data collection

9.Feng-Chiao Huang– Data collection

10.Chia-Jen Liu,Tsun– Data collection

11.Cheng Huang– Data collection

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