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Disparity in attitudes regarding assisted dying among physicians and the general public in Japan

Yoshiyuki Takimoto[1*] and Tadanori Nabeshima[2]

Abstract

Background Recently, an increasing number of countries have been allowing voluntary active euthanasia (VAE) and physician-assisted suicide (PAS) as part of palliative care. Japan stands out as the most aged country in the developed world, and while the need for palliative care for older adults with dementia has been noted, there has been reluctance to openly address VAE and PAS.

Methods We conducted an online questionnaire survey using a vignette case to investigate the attitudes of Japanese physicians and the general public towards VAE and PAS, and the factors influencing these attitudes.

Results The findings revealed that Japanese physicians did not display support for euthanasia (2%) and assisted suicide (1%); however, the general public supported euthanasia (33%) and assisted suicide (34%). Notably, among the general public, males exhibited significantly higher support for PAS than females.

Conclusion Japanese physicians and the general public expressed a more negative stance towards VAE and PAS compared with their counterparts in Western countries. This disparity may be attributed to the influence of the Buddhist view of life and death and family-centeredness in the Japanese culture, which affects people's attitudes towards assisted dying. The gap between physicians and the general public could potentially lead to challenges in medical practice, thereby, necessitating the need for open discussions in the future.

Keywords Assisted dying, Voluntary active euthanasia, Physician-assisted suicide, Palliative care

Introduction

Japan has the largest aging population amongst the world's developed countries, thus highlighting the need for palliative care for dementia and other conditions within the older adult population [1]. According to the European Association of Palliative Care, assisted dying encompasses both voluntary active euthanasia (VAE), where 'a doctor intentionally kills a person by the administration of drugs', and physician-assisted suicide (PAS), where 'a doctor helps a person to commit suicide by providing drugs for self-administration' [2]. Whilst some medical conditions lead people to believe requirement VAE and PAS, there is an ongoing ethical debate surrounding these practices [3], which are illegal in many countries. Nonetheless, VAE is currently legal in seven countries and PAS in nine countries, including certain states in the United States [4, 5]. VAE and PAS are approved in some Western countries, without necessarily being applied to terminal patients [5]. Attitudes

*Correspondence:
Yoshiyuki Takimoto
takimoto@m.u-tokyo.ac.jp
[1]Department of Biomedical Ethics, Faculty of Medicine, The University of Tokyo, Tokyo, Japan
[2]Department of Emergency and Critical Care Medicine, Tokyo Bay Urayasu Ichikawa Medical Center, Tokyo, Japan

towards VAE and PAS have been extensively reported in the United States and Europe since the 1990s, revealing increasing public support for these practices in Western Europe but a slight decrease in the United States and Eastern Europe [4].

Physicians generally exhibit less support for VAE and PAS than do the general public [4]. However, the former have diverse attitudes towards VAE. In Belgium and the Netherlands, where VAE is legal, most physicians believe that VAE and PAS are justified in certain circumstances [6, 7]. Conversely, in Italy, which has not legalised these measures, only 36% of doctors endorsed VAE in 2018 [8]. However, there has been noted a gradual increase in physicians' acceptance of these practices in countries where VAE and PAS are currently illegal. A recent Swedish study demonstrated a clear shift towards a more accepting attitude, with 47% of physicians supporting PAS in 2020 compared with 35% in 2007 [9]. Furthermore, Louhiala et al.'s [10] study of Finnish physicians reported a growing acceptance of VAE over the past decade. Although the World Medical Association considers euthanasia unethical [11], there is a rising acceptance of the concept of assisted dying, both amongst the general public and physicians.

This change has been attributed to the influence of cultural worldviews on the attitudes of physicians, patients, and patients' families towards euthanasia [12]. Therefore, Japan and other Asian countries may exhibit distinct reactions to VAE and PAS compared with Western countries. Despite undergoing Westernisation, many Asian countries, including Japan, continue to be heavily influenced by Confucianism and Buddhism, displaying varied perspectives. A recent report indicates that approximately 60% of medical students in Hong Kong hold negative attitudes towards euthanasia and assisted suicide [13].

In Japan, VAE and PAS remain illegal, and there exists a reluctance to openly discuss these topics [14]. Japanese people shy away from conversations about death, often preferring *Omakase* (leaving it up to others) and choosing not to participate in decisions about their own death [15]. In addition, discussions surrounding end-of-life care primarily involve healthcare providers and patients' families, often excluding the patients themselves [16]. In Japan, euthanasia is divided into 'passive' euthanasia, which involves withholding and withdrawing life-sustaining treatment, and 'active' euthanasia, where the physician intentionally causes the patient to die. Internationally, the term euthanasia means 'active' euthanasia that is VAE, and 'Withdrawing and Withholding' treatments is commonly used as a term to mean 'passive' etuhanasia. There are clear ethical differences between 'active' and 'passive' euthanasia. Surveys on the attitudes of physicians and the general public towards euthanasia have primarily focused on 'passive' euthanasia; however, their attitudes towards VAE and PAS remain unknown. The current study fills this gap by conducting a questionnaire survey using vignette cases. In addition, the study examines the potential influence, on these attitudes, of factors such as age, gender, marital status, presence of children, presence of disease, and caregiving experience.

Methods

We conducted a web-based survey [17] amongst Japanese citizens and physicians, using a questionnaire with two vignettes centred around VAE and PAS. The general public sample comprised individuals registered with a marketing research company. The sample of the general public was selected to target adults and closely match the age and gender distribution of the Japanese population. The survey for citizens was conducted in March 2021. The total number of samples required for statistical analysis was 262, determined through the POWER procedure of SAS by setting a difference of 20 points in accordance with previous studies (Ruhnke et al. 2000), with $\alpha = 0.05$ and $\beta = 0.1$. All in all, 1,200 citizens were asked to respond to the survey as we aimed to obtain 400 responses. A total of 5,892 physicians affiliated with the Japan Primary Care Association—a primary care society—and 3,280 physicians affiliated with The Japanese Society of Intensive Care—an intensive care society—were invited via email mailing lists maintained by these professional societies to respond to the web-based questionnaire. A survey of physicians was conducted in February 2022.

Vignette case

Detailed medical information was not included in the vignettes so as to ensure consistency in the survey content provided to the public. The vignettes were revised based on feedback from two physicians (one psychiatrist and one cardiologist), two nurses, and two administrative staff members who responded to a pre-study survey to determine whether the content was comprehensible. Both the citizen and physician groups were asked to indicate how they would act if they were the physician in the case. The questions were presented randomly so as to prevent participants from being influenced by the answers to the previous questions.

Statistical analysis

For the statistical analysis, we generated cross-tabulation tables for each vignette and performed the Fisher's exact test to determine significant differences between both groups' responses. To account for multiple comparisons, the Bonferroni method was used to adjust each p-value in the results. Binomial logistic regression analysis was conducted to test the association between family-centred attitudes and age, gender, marital status, presence

of children, disease status, and caregiving experience. All the variables were included as forced entries. All statistical analyses were two-tailed and a p-value of <0.05 was considered statistically significant.

Results

Participants

The final respondent sample comprised 457 members of the public (226 men and 231 women), with a response rate of 38%. The participants ranged from their 20s to their 60s. Approximately half were married and half had children. Of the public respondents, 11% were undergoing treatment for a disease and 21% had caregiving experience (Table 1).

Additionally, 284 physicians (209 men and 75 women) responded to the survey, with a response rate of 3%. The largest proportion of physicians (35%) had over 19 years of professional experience, and 33% had 11–18 years of experience after obtaining their medical specialty certification. Overall, 79% of the physicians were married and 65% had children. In addition, 16% had a disease for which they were undergoing treatment and 17% had experience as caregivers.

Voluntary active euthanasia

Among the physicians, only 2% supported VAE, unlike one-third of the citizens who supported it, showing a significant difference in their attitudes towards VAE ($p<0.001$) (Table 2).

Patient-assisted suicide

Only 1% of the physicians supported PAS, as opposed to one-third of the citizens who supported it, illustrating a significant difference in their attitudes towards PAS ($p<0.001$) (Table 2).

Factors influencing the citizens' support for VAE and PAS

No factors, including age, marital status, presence of children, caregiving experience, and presence of disease, significantly influenced citizens' support for VAE and PAS (Table 3), except for gender. However, PAS was significantly endorsed by male participants compared with female participants (OR = 1.64, $p=0.02$).

Discussion

In countries where assisted dying is legal, certain conditions need to be met for it to be approved. These include the patient being in the terminal stage of illness,

Table 1 Participant characteristics

Citizens ($n=457$)						
Age (years)	20–29	30–39	40–49	50–59	60–69	
	88 (19%)	92 (20%)	93 (20%)	88 (19%)	96 (21%)	
Gender	Male		Female			
	226 (49%)		231 (51%)			
Marital status	Yes		No			
	263 (58%)		194 (42%)			
Children	Yes		No			
	228 (50%)		229 (50%)			
Diseases under treatment	Yes		No			
	52 (11%)		405 (89%)			
Care experience	Yes		No			
	96 (21%)		361 (79%)			
Physicians ($n=284$)						
Physician experience (years)	≦6	7–10	11–18	19≦		
	42 (15%)	48 (17%)	94 (33%)	100 (35%)		
Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
	28 (10%)	100 (35%)	80 (28%)	51 (18%)	23 (8%)	2 (1%)
Gender	Male		Female			
	206 (73%)		78 (27%)			
Marital status	Yes		No			
	237 (79%)		57 (21%)			
Children	Yes		No			
	185 (65%)		99 (35%)			
Diseases under treatment	Yes		No			
	45 (16%)		239 (84%)			
Care experience	Yes		No			
	48 (17%)		236 (83%)			

Table 2 Attitudes of physicians and citizens towards the explanation of medical conditions

Case A. The patient has terminal cancer and has less than six months to live. The patient will gradually become weaker, unable to take care of him/herself, and unable to speak. In the worst-case scenario, the pain will become worse, and it will be difficult for him/her to maintain his/her identity. The patient and their family discussed the situation thoroughly and concluded that if the patient could no longer endure the physical and emotional pain, they wanted the patient to die whilst still being able to maintain their identity and be cared for by their family. The doctor was asked by the patient and his family to use a drug that will end his life in case the worst should happen.
Question:
As the patient's doctor, which action would you choose to take?
a. Respect the patient and family's wishes to administer lethal drugs.
b. Lethal drugs are not administered.

	Citizen	Physician
Respect the patient and family's wishes to administer lethal drugs.	152 (33%)	5 (2%)
Lethal drugs are not administered.	305 (67%)	279 (98%)
Fisher's exact test *p*-value	$p < 0.001$	

Case B. The patient has terminal cancer and has less than six months to live. The patient will gradually become weaker, unable to take care of him/herself, and unable to speak. In the worst-case scenario, the pain will become worse, and it will be difficult for him/her to maintain his/her identity. The patient and their family discussed the situation thoroughly and concluded that if the patient could no longer endure the physical and emotional pain, they wanted the patient to die whilst still being able to maintain their identity and be cared for by their family. The patient and his family asked the doctor to prescribe a life-ending medication, which the patient could take independently in case the worst should happen.
Question:
As the patient's doctor, which action would you choose to take?
a. Respect the patient and family's wishes to prescribe lethal drugs.
b. Do not prescribe lethal medications.

	Citizen	Physician
Respect the patient and family's wishes to prescribe lethal drugs.	156 (34%)	3 (1%)
Lethal medications are not prescribed.	301 (66%)	281 (99%)
Fisher's exact test *p*-value	$p < 0.001$	

Table 3 Factors influencing Voluntary Active Euthanasia (VAE) and Physician-Assisted Suicide (PAS) in the general population

Case	Gender (M or F) Ref Male		Age		Married (Yes or No) Ref No		Children (Yes or No) Ref No		Experience in caregiving (Yes or No) Ref No		Diseases under treatment (Yes or No) Ref No		Hosmer-Lemeshow test
	Odds (CI)	*p*	Odds (CI)	*p*	Odds (CI)	*p*	Odds (CI)	*p*	Odds (CI)	*p*	Odds (CI)	*p*	*P*-value
VAE	0.84 (0.57–1.25)	0.39	1.05 (0.91–1.21)	0.54	1.15 (0.69–1.9)	0.59	1.26 (0.76–2.08)	0.38	1.02 (0.62–1.68)	0.94	0.95 (0.5–1.81)	0.89	0.49
PAS	**0.61** (0.41–0.91)	**0.02**	1.06 (0.92–1.23)	0.42	1.08 (0.65–1.79)	0.77	1.51 (0.91–2.51)	0.11	1.17 (0.7–1.96)	0.55	1.02 (0.54–1.94)	0.94	0.25

Pt = patient-centred, Fm = family-centred, M = male, F = female, p = *p*-value, CI = 95% confidence interval

experiencing uncontrollable pain, and the patient's wishes being clear. In the vignette case used in this study, these conditions were met. Of note here is a study which investigated how physicians and medical students distinguished between 'killing' and 'letting die' in end-of-life cases [18]. The results indicated that, if the patient consents, then the doctor's actions, whether administering a lethal drug or withdrawing treatment, tend to be regarded as not causing the patient's death, and the doctor is not held liable for having killed the patient. Considering these findings, in the vignette case used in this study, where the patient's wishes were clear, it would be difficult for the respondents to argue that the doctor's actions caused the patient's death. Moreover, in the vignette case, both the patient and their family consented

to assisted dying. This would cause less trouble in Japan, where the population is family-centred [17, 19] and the conditions for choosing VAE or PAS are more likely to be met.

Nevertheless, the Japanese physicians in this study unanimously disapproved of VAE or PAS. Although the surveys conducted in the US, Europe, and Australia consistently show lower physician support for VAE and PAS compared to the general public [6, 10, 20–26], it is not as low as in Japan. For example, in a 2014 survey regarding whether PAS should be allowed, conducted amongst physicians in seven countries ($n = 21,531$), physicians from the US were the most supportive (54%), followed by Germany (47%), the United Kingdom (47%), Italy (42%), Spain (36%), and France (30%) [27]. Although this survey did not present specific cases, it reflected an ethical perspective regarding the allowance of PAS.

Studies have shown that regional and cultural differences are more likely to be reflected in questions regarding actual behaviour rather than in ideal ethical decisions [28, 29]. In this study, the questions focused on actual behaviours with a view to gaining insights into the real, rather than ideal, attitudes of physicians. Japanese physicians could have been more supportive of VAE and PAS if they were asked about their ideals, as observed in previous studies. Nevertheless, Japanese physicians' complete rejection of VAE and PAS stands out in comparison to their European and American counterparts.

This rejection could be due to several possible factors. First, there may be a strong reluctance to implement VAE or PAS because of the perceived legal risks. In Japan, the Yamauchi and the Tokai University Hospital cases have demonstrated the criteria for active euthanasia [30]; however, the Ministry of Health, Labor, and Welfare does not approve of active euthanasia, placing Japanese physicians in an ambivalent position regarding the matter [31]. Under the Japanese Penal Code, assisting suicide is considered a criminal offense. Therefore, along with VAE and PAS, the withdrawal of life-sustaining treatment could potentially be considered a crime [31]. Japan has observed cases wherein doctors who have performed VAE, including the withdrawal of life-sustaining treatment, have been prosecuted and found guilty of murder [32].

Second, the physicians surveyed may have determined that the vignette cases did not fully meet the conditions for VAE or PAS to be legally permissible. In the two vignette cases, the patients were in the terminal stages of illness, experiencing uncontrollable and unbearable physical pain, and the wishes of the patients and their families were clear, fulfilling the criteria for VAE or PAS [5, 33]. However, in countries where these practices are legal, additional requirements are often imposed, such as a documented will and verification by a third-party physician, confirming that the conditions meet the eligibility criteria for VAE or PAS [5]. As the vignette cases do not meet al.l these additional conditions, the physicians may have been reluctant to choose VAE or PAS. Nonetheless, the lack of attention to VAE and PAS amongst physicians in Japanese clinical practice suggests that the respondent physicians may be unaware of the specific conditions outlined in countries where VAE and PAS are legal.

Third, Japanese physicians may exhibit a stronger tendency than their American and European counterparts to avoid causing harm to the lives or health of their patients through their actions. Japanese medical practice is considered more paternalistic than practices in the United States and Europe [34, 35]. The principle of beneficence, which emphasises medical benefit, and the principle of non-maleficence, which emphasises the importance of avoiding harm to the patient, support a paternalistic tendency [36]. Thus, Japanese medical practice emphasises the principle of non-maleficence, which is further suggested by the fact that Japanese physicians may withhold treatment but harbour a negative attitude towards the withdrawal of treatment [37]. In addition, a previous study examining the attitudes of Australian and Japanese nurses towards active euthanasia reported that 85% of the Japanese nurses considered the wish for euthanasia reasonable in some cases, yet only 14% (compared with 65% in Australia) expressed their willingness to practise active euthanasia even if it were legal [38]. This suggests that Japanese medical practitioners value the principle of non-maleficence.

In the current study, approximately 30% of the general public expressed support for VAE and PAS. Similarly, in a previous study, approximately 46% of 2,548 Japanese citizens reported that they would prefer VAE in the presence of intractable, intense cancerous somatic pain [39]. However, the previous survey's question lacked specificity, focusing on personal wishes as patients, rather than physicians' actions. Consequently, the number of people supporting VAE was 1.5 times higher than that found in the present study, which specifically asked whether participants, as physicians, would practise VAE.

A recent survey conducted in South Korea, a country which has cultural similarities with Japan, revealed that 74.6% of the general public favoured the legalisation of euthanasia, indicating the growing support for VAE and PAS, similar to the United States and European countries [40]. In South Korea, influenced by socio-economic factors, the increasing awareness regarding self-determination in end-of-life decision-making [41] may explain the higher support for VAE and PAS based on the Western notion of respect for autonomy. However, in Japan, the awareness of self-determination in the end-of-life period

remains low [17], which could explain the lower support for VAE and PAS in the country.

In this study, citizens were significantly more supportive of VAE and PAS than doctors. One reason the general public supports VAE and PAS more than doctors may be that the public confuses the withdrawal of life-sustaining treatment with active euthanasia. This may be related to the fact that in Japan, the term '*Songenshi*', which means death with dignity, is widely used among citizens instead of euthanasia. The term '*Songenshi*' was popularized by the Japan Society for Dying with Dignity—originally the Japan Society for Euthanasia at its founding in 1976—which used the term '*Songenshi*' to include VAE and PAS. Although in 1991, the meaning of '*Songenshi*' was changed to refer only to the withdrawal of life-sustaining treatment—or 'passive' euthanasia—the general public may still perceive active and passive euthanasia as a single concept under the term '*Songenshi*', without distinguishing between them.

One possible reason for the lack of support for euthanasia and assisted suicide among both physicians and the general public in this survey, compared with that in Western countries, could be the conflicting perceptions of death in Japan. In medieval Japan, suicide was considered an honourable death, as symbolised by the samurai code of bushido, and death was taken lightly during wartime. Consequently, a noteworthy study suggested that a stronger aversion to death emerged in the post-war period [42]. This conflict regarding death is recognised in Buddhism, which has considerably influenced the Japanese culture. Whilst some scholars argue that Buddhism is sympathetic towards euthanasia and compassionate killing [43], euthanasia and suicide are explicitly prohibited in Buddhist texts, even in cases involving autonomy and suffering [44]. Furthermore, patients in Asian countries often seek meaning in life and death, influenced by Buddhism and other belief systems, leading them to prioritise the preservation of life even during the end-of-life stage [12, 45]. Although 30% of Japanese people practice Buddhism, it is considered a customary belief and they may not fully understand Buddhist concepts [46]. Individuals with a deep understanding of Buddhism may think that Buddhism does not necessarily prohibit choosing one's own death, while those who follow customary beliefs in large numbers may consider 'choosing one's own death as a sin.' Investigating whether there are differences in views on active euthanasia and physician-assisted suicide based on the degree of Buddhist faith and the understanding of Buddhim seems to contribute to clarifying this point.

The current study revealed a significant gender difference amongst the Japanese general public regarding the preference for PAS, with men being more likely to choose it than women. This is in line with the findings in the United States, where support for VAE and PAS has been associated with men, younger adults, and individuals with lower religious affinity [47–54].

The difference in support for VAE and PAS between men and women might be explained by the gender differences observed in response tendencies to the 'trolley moral dilemma', as the topic of the current study raises similar ethical dilemmas [55]. In previous studies, men have been found to respond to the 'trolley moral dilemma' in a utilitarian manner, whereas women respond in a deontological manner [56, 57]. Active euthanasia and assisted suicide, even if aligned with the patient's wishes and for their benefit, are acts that intentionally cause a person's death, which can be criticised from the standpoint of Kant's theory of deontology. Women have been reported to make deontological choices because of harm and action aversions [58]. Therefore, in moral dilemmas involving life and death, women, with their deontological tendency, are less likely than men, who exhibit a utilitarian tendency, to deliberately choose an action that causes death. Another study suggested that gender differences in such dilemmas arise from emotional prominence [59]. Of note is the fact that both VAE and PAS are actions that elicit emotional resistance from the person who commits them; indeed, this could explain why women are less inclined to choose them. The aforementioned mechanisms of moral judgment, characterised by the dual process, are known to have cross-cultural characteristics [60]. The gender differences found in Japan and the United States support the existence of these mechanisms.

In the current study, younger participants did not exhibit a tendency to choose active euthanasia or assisted suicide, contrasting with the findings from the United States. Previous studies have indicated that younger people are more likely to ma4e utilitarian choices in personal moral dilemmas that involve potential psychological resistance [61]. Both VAE and PAS are similar to personal moral dilemmas in that they involve direct actions that cause the patient's death. Therefore, younger people are typically more supportive of VAE and PAS than are older people. However, in Japan, decision-making based on the Confucian ideology, which emphasises human relationships, is preferred [12], suggesting a strong tendency towards family-centredness and respect for elders [62]. A survey conducted in Japan amongst children of terminally ill patients found that 43% of the respondents believed it was their filial duty to do everything possible to keep the patient alive [63]. Thus, the belief that a patient's death involves the entire family, rather than solely the individual patient, contributes to a culture of family-centredness and influences end-of-life treatment decisions, presumably resulting in a different trend than in the United States. Conversely, a previous survey conducted amongst bereaved families of patients who died in palliative care units in Japan reported that bereaved

families (those members aged under 60) and unrelated relatives were more likely to support the legalisation of euthanasia [64]. The study suggested that younger individuals in Japan may be more supportive of euthanasia, similar to the United States. The disparity in results between this study and previous studies may be attributed to the fact that the latter involved bereaved families of hospice patients – a group more likely to have positive views regarding euthanasia – and so there may be a gap between supporting euthanasia legalisation and approving its practice on patients.

In Japan, a stark contrast has been observed between the negative stance of physicians towards VAE and PAS, and the willingness of a certain portion of the general public to choose these options. Currently, in clinical practice in Japan, patients rarely ask physicians to perform VAE or PAS. However, a survey of 3,299 oncologists in the United States reported that 56% of them had received requests for PAS and 38% for VAE [33], whereas a survey of 1,456 physicians in the Netherlands reported that 77% of them had received VAE or PAS requests [7]. In an earlier Japanese survey, 28% of the doctors and nurses caring for terminally ill cancer patients had experienced situations where patients in severe pain expressed a desire to end their lives and the families supported the patients' decision [14]. Even amongst the general public, one-third of individuals who are not terminally ill cancer patients support VAE and PAS. As the Japanese population ages further, physicians are expected to receive more requests for VAE or PAS from patients and their families in the future. Such requests can place a significant emotional burden on the physicians, as suggested by a 2011 survey of Dutch physicians ($n = 1456$), where 86% of the physicians expressed fear regarding the emotional impact of performing VAE [65]. Considering the current situation in Japan, where physicians do not support VAE or PAS, the disparity in attitudes between physicians and the general public may cause tension in Japanese clinical practice in the coming years.

Limitations

Despite its contributions, this study has several limitations. First, the potential influence of framing effects cannot be ruled out in studies that investigate attitudes. Endorsement of euthanasia can vary substantially depending on the wording of the survey questions, provision of specific patient details, prognosis, medical diagnosis, symptoms, characteristics of intervention methods, and whether the focus is on ethical acceptability, legalisation, or other endorsements [4]. Second, the response rate of physicians was low, owing to the limited response period of the web survey, thereby limiting the generalisability of the results. Third, the underlying reasons for the attitudes towards VAE and PAS were not confirmed. Conducting qualitative research could help to clarify the factors which contribute to such attitudes.

Conclusion

Japanese physicians surveyed demonstrated a complete lack of support for VAE and PAS. Although the general public exhibited less support compared with Europe and the United States, approximately 30% of them still supported these practices, highlighting a significant gap between physicians and the general public. VAE and PAS pose various ethical [3] and practical [5] challenges. However, considering the extent of public support, irrespective of whether VAE or PAS should be performed in Japan, their ethical and legal aspects ought to be widely discussed based on Japan's unique perspective on life and death.

Author contributions

Y.T. planned the research project and analyzed the data. Y.T. wrote the main manuscript text. T.N. collected the data.All authors reviewed the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee in The University of Tokyo (Date 1/22/2021 /No 2021325NI-(1)).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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