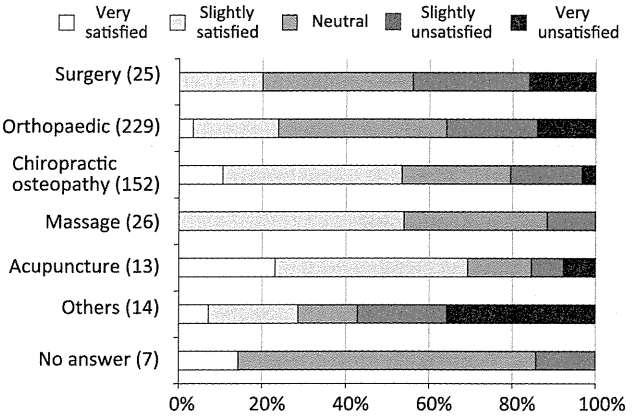

Fig. 5 Patient satisfaction with initial treatment, by type of treatment facility

those reporting pain in the 2010 survey said that the pain had persisted for 3 years or longer.

This study identified the following risk factors for the new development of chronic pain: female gender, occupation (professional, managerial, clerical/specialist), a BMI ≥25, current use of alcohol, current use of cigarettes, and completing an education level of vocational school or higher. As many diseases are associated with low socioeconomic status [3], it is very interesting that chronic pain was instead associated with high socioeconomic status, including professional occupations, and higher levels of education. By occupation, managerial, professional, and technical work categories had the highest incidence. The lower back was the most frequently reported site of pain. Previous studies demonstrated that occupational factors, such as long periods of sedentary posture and psychological factors due to dissatisfaction with a work situation, a supervisor, or a dead-end job and boredom, appear to promote the development of new chronic pain [4, 5]. Furthermore, the recent studies demonstrated that the psychosocial factors play important roles in chronic musculoskeletal pain [6–8]. Because the limitation of the present study was that the psychosocial factors were not examined, further study should be performed to clarify the

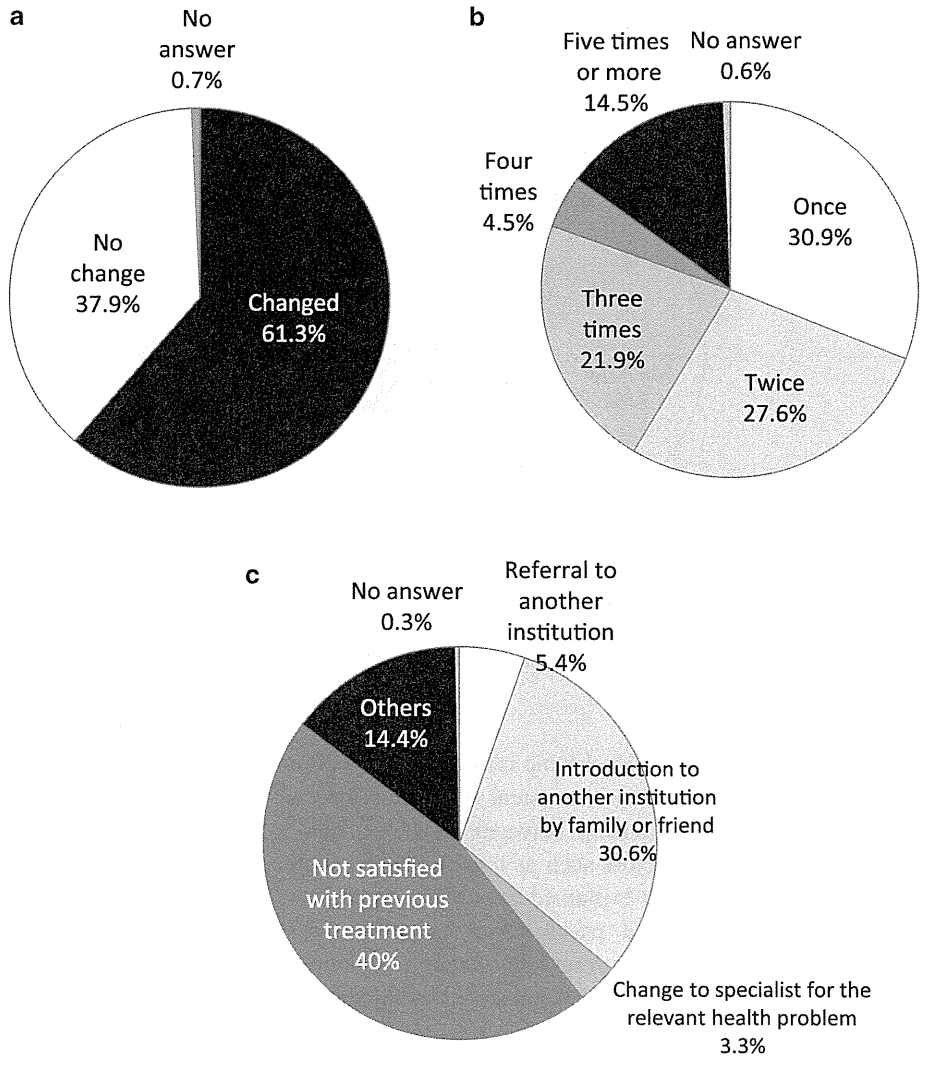

Fig. 6 Circumstances of changes in treatment facility: **a** whether changed, **b** number of changes, and **c** reason for changing

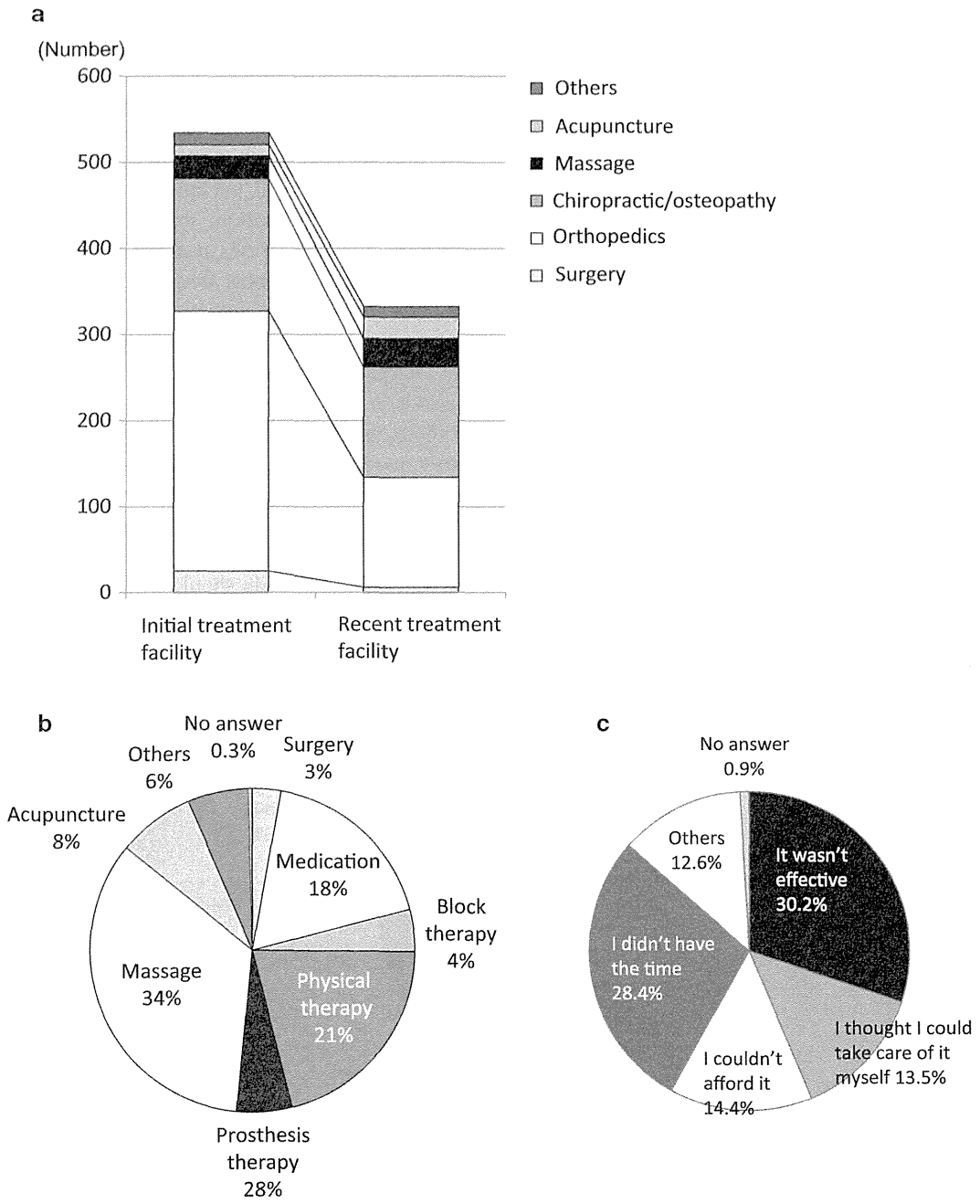

Fig. 7 Details of changes in treatment facility: **a** initial and most-recent treatment facility, **b** type of most recent treatment, and **c** reason for discontinuing treatment

effects of these factors on the chronic musculoskeletal pain in the future. Taken together, consistent with the previous studies [9–12], the relationship between musculoskeletal pain and the identified factors such as female gender, high BMI and smoking may be explained in part by shared risk factors, both physical and psychosocial [13, 14]. The mechanism involved in the current identification of alcohol use as a risk factor for new development of chronic pain is unknown.

Persistence of chronic musculoskeletal pain

The results showed that 45 % of the respondents who reported chronic pain in 2010 also reported chronic pain in 2011. It is possible that people who suffered from chronic pain through the entire period were more inclined to reply to the second questionnaire; thus, we cannot rule out the possibility that 45 % is an overestimation, even though the reply rate was 85 %. Multivariate analysis did not find any

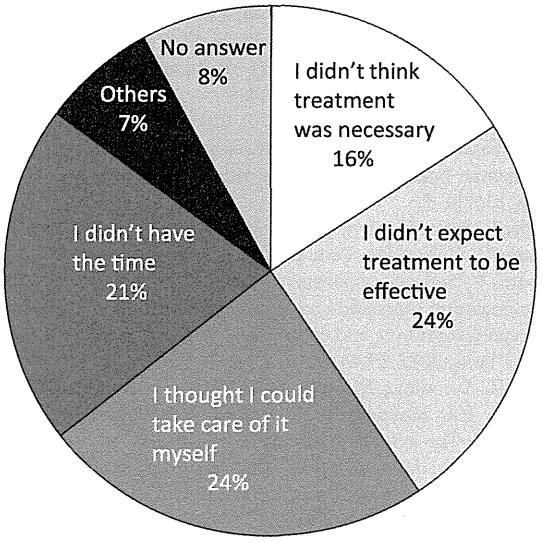

Fig. 8 Reasons given for not seeking treatment for persistent chronic pain

associations between the persistence of chronic pain and basic attributes such as age and gender; the only associated factors were related to the pain itself. A pain severity VAS score of 7–8 was statistically significant. Although the odds ratio increased to 1.30 with the more severe pain reflected in VAS scores of 9–10, it did not reach statistical significance, perhaps because the sample size for this group was so small. The risk of chronic pain persisting a year later was twice as high among persons who had complained of constant pain compared to those who had reported a frequency of 2–3 times a week. The odds ratio for pain persistence was significantly higher for those who reported pain lasting 5 years or more. Based on these findings, those with constant, severe pain persisting 5 years or more appeared to be at the highest risk for the persistence of chronic pain 1 year later. These findings suggested that once the pathological condition of chronic musculoskeletal pain has been established, it could be quite difficult to relieve the chronic musculoskeletal pain. The risk of pain persisting was particularly high for those whose chief complaint was low back pain, compared to pain at other sites. Countermeasures to prevent chronic pain appear to be especially important for these high-risk populations.

Problems in treating persons with persistent chronic pain and countermeasures

More than 8 out of 10 people with persistent chronic pain had a history of treatment, and while 3 of the 8 were still receiving treatment at the time of the survey, the other 5 had discontinued treatment despite the persistence of pain. Of those who had been treated for pain, 60 % were initially treated at a medical facility; these respondents reported a low degree of satisfaction even though 75 % had received frequent (daily or several times a week) treatment, and 40 % had been treated long-term (a year or more). Of particular note, results by type of treatment provider showed that respondents were less satisfied with treatment received at medical facilities than with folk medicine treatment. We thought that differences in pain severity might be responsible for this finding, but the average VAS scores of those treated at medical facilities and those treated with folk medicine were 6.0 and 5.7, respectively, and this difference was not statistically significant. Other factors might include a tendency toward unrealistically high expectations of medical facilities, and less communication and physical contact in comparison with folk medicine methods. Additional surveys will be necessary in order to verify these factors.

More than 60 % of the respondents with persistent chronic pain had changed their treatment facility; of these, approximately 60 % had changed once or twice. Surprisingly, 15 % of the respondents with persistent chronic pain changed 5 or more times, engaging in so-called "doctor shopping". A review of the initial and most-recent treatment facilities showed that approximately half of those initially examined in an orthopaedics department changed treatment facilities, but no major change was seen in those initially examined for folk medicine treatment. The results by type of treatment also showed that the use of massage and acupuncture/moxibustion increased, accounting for 42 % of the most-recent treatment types reported. This is consistent with the finding of a low degree of satisfaction with treatment at medical facilities. The recent nationwide survey of chronic pain sufferers in Japan also demonstrated they did not have a high degree of satisfaction with medical treatment [15].

The most common reason given for changing treatment providers or discontinuing treatment was, "because the treatment was ineffective", which reflects the inadequate effectiveness of the current treatments for chronic musculoskeletal pain. Nociceptive pain, neuropathic pain, and psychogenic pain are intermingled in chronic musculoskeletal system pain, and neuropathic pain is involved in chronic low back pain in particular [16]. Without an adequate grasp of the roles these factors play in the pathology of pain, treatment may fail because it is not appropriate for the patient. Furthermore, the recent studies demonstrated that the psychosocial factors play important roles in chronic musculoskeletal pain [13, 14]. Because the limitation of the present study was that the psychosocial factors were not examined, further study should be performed to clarify the effects of these factors on the chronic musculoskeletal pain in the future.

Many people with persistent chronic pain discontinued treatment. Others did not seek treatment, giving reasons

such as not having time, thinking they could take care of it themselves, not thinking they needed treatment, and so on. The majority of the respondents who were not treated for pain reported using non-prescription drugs to cope with the pain. Thus, poor recognition of the seriousness of chronic pain appears to be a problem. It is reported that chronic musculoskeletal pain takes a toll on both mental and physical health, and strongly impacts daily and social life [2]. However, it cannot be said that this state of affairs has been adequately conveyed to the Japanese public. We orthopedists, who specialize in treating the musculoskeletal system, have before us the important task of finding ways to reliably convey the importance of treating chronic pain, to both patients and the general public, through public awareness campaigns.

Acknowledgments This study was conducted as a 2011 Ministry of Health, Labour and Welfare Health Labour Sciences Research Grant for Comprehensive Research on Disability Health and Welfare (Survey study of chronic musculoskeletal pain).

Conflict of interest The authors declare that they have no conflict of interest.

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J Orthop Sci
DOI 10.1007/s00776-014-0567-6

ORIGINAL ARTICLE

Investigation of chronic musculoskeletal pain (third report): with special reference to the importance of neuropathic pain and psychogenic pain

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Received: 29 January 2014 / Accepted: 4 March 2014

Abstract
Background The previous epidemiological surveys conducted in Japan revealed that once the vicious cycle of chronic musculoskeletal pain begins, it is difficult to disrupt the cycle. This finding suggests the existence of problems with the conventional approaches to treatment of chronic musculoskeletal pain. The purpose of this study was to investigate the characteristics of patients with chronic musculoskeletal pain focusing on neuropathic and psychogenic pain.

Methods The questionnaire was sent again to the 660 subjects found to have persistent chronic pain in the epidemiological surveys conducted in 2011. Responses were collected from 588 subjects (response rate 90 %).
Results Of the 588 responders, 365 (62 %) complained of persistent chronic pain. Among them, 128 (35 %) were still receiving treatment and 193 (53 %) had discontinued treatment. The degree of satisfaction with the treatment was low, and 66 % of the patients had switched the medical facility that they visited to receive treatment. The cited reasons for the change in the medical facility visited and discontinuation of treatment were "treatment was ineffective," "I did not have sufficient time," "I thought I could take care of it myself," and "Treatment seemed to be unnecessary". Involvement of neuropathic pain was suggested in 20 % of all the patients with chronic pain. As the PainDETECT Score rose, the Visual Analog Scale (VAS) score became higher and the change of medical facility for treatment also increased. The Pain Catastrophizing Scale score was correlated positively with the VAS score. The Hospital Anxiety and Depression Scale score was significantly correlated with the VAS score and the duration of pain.
Discussion The results of this survey indicated that the chronic course of musculoskeletal pain may be attributable to the following factors: (1) lack of appropriate treatment of neuropathic pain and psychogenic pain, and (2) insufficient awareness/knowledge among patients about chronic musculoskeletal pain.

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Introduction

The National Livelihood Survey provides data on symptoms currently prevalent in the Japanese general

Published online: 16 April 2014

population. According to this survey, low back pain, shoulder stiffness, joint pain and other types of pain are highly ranked [1]. However, while attempting to devise countermeasures against chronic pain among Japanese people, we faced shortage of even basic information concerning the types of pain. Taking this background into account, we initiated the "longitudinal investigation of chronic musculoskeletal pain" in 2010. Until date, we have reported, based on the results of this survey, the prevalence of chronic musculoskeletal pain (15.4 %), the frequency of new onset of this type of pain (11.1 %), and the risk factors for the onset of chronic pain in the Japanese population. The investigation additionally revealed that chronic pain was frequently persistent (45.2 %), and that the risk factors for persistent pain were a VAS score of $\geq$7, duration of pain of $\geq$5 years, and pain affecting the lower back. Of the responders complaining of persistent chronic pain, more than 80 % had a history of treatment; about 30 % were still receiving treatment at the time of the investigation, while 50 % had discontinued treatment because of poor satisfaction with the outcome of treatment [2, 3]. These findings suggest that once the vicious cycle of chronic musculoskeletal pain begins, it is difficult to disrupt the cycle, and that the conventional approaches to treatment of chronic musculoskeletal pain may involve problems. The present survey was undertaken in the same subjects as those in the previously performed mail-based survey to characterize them with a chronic course of musculoskeletal pain, with emphasis laid on the possible involvement of neuropathic pain or psychogenic pain, and identification of problems with the conventional approaches to treatment.

Methods

The questionnaire was mailed to 660 subjects who complained of persistent chronic pain in both the epidemiological surveys of 2010 and 2011 according to the mail-based survey panel maintained by Nippon Research Center, Ltd. [2, 3]. Responses were collected from 588 subjects

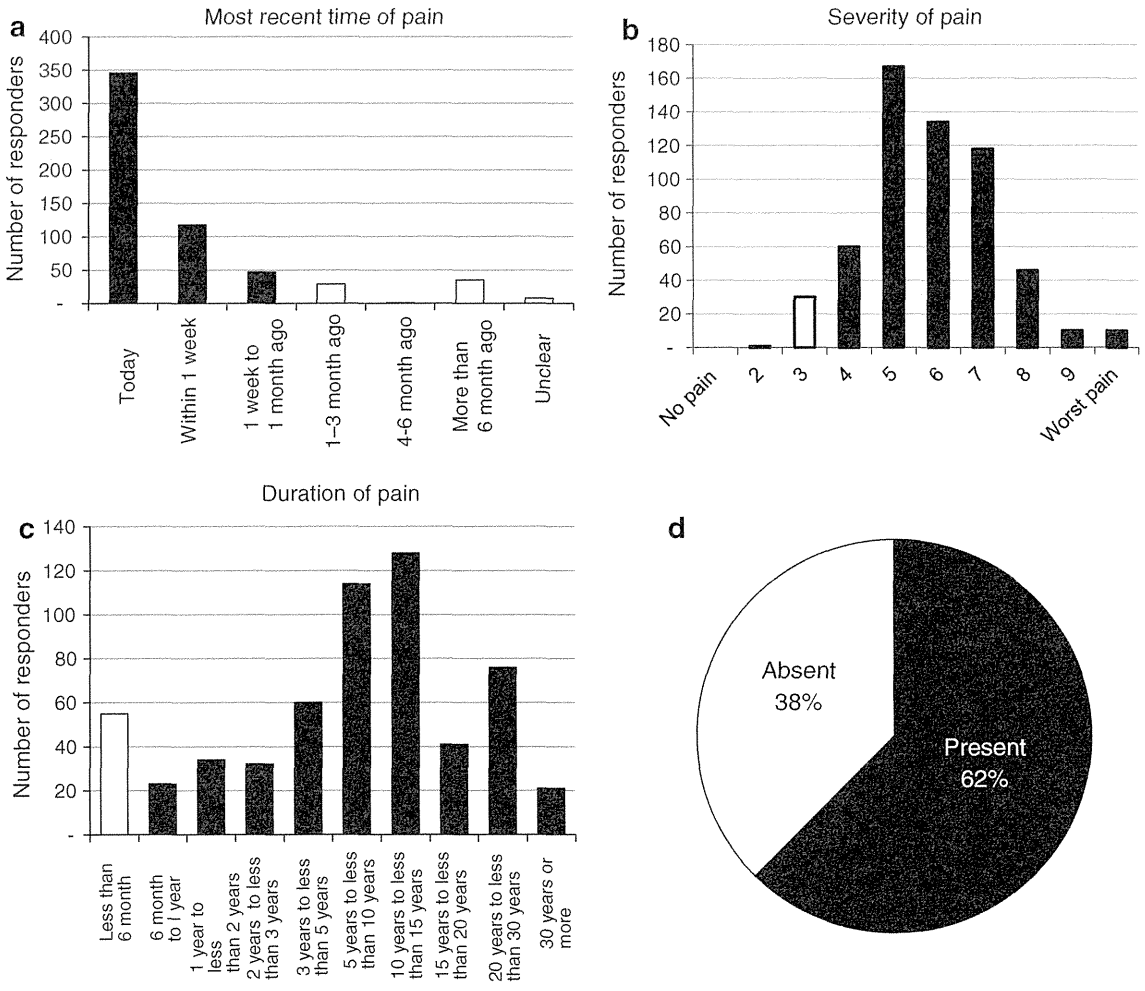

Fig. 1 **a** Most recent time of pain, **b** severity of pain (visual analog scale), **c** duration of pain, **d** prevalence of chronic musculoskeletal pain

(response rate, 90 %). The questionnaire used in this survey contained questions to determine information on the basic demographic characteristics of the subjects (gender, age, location of living, occupation, etc.), information about the chronic musculoskeletal pain (severity, location, duration, presence/absence of treatment, treating medical facility, therapeutic regimen used, treatment period, efficacy, degree of satisfaction with treatment), and information about neuropathic pain (PainDETECT score) [4] or psychogenic pain (Hospital Anxiety and Depression scale: HADS, Pain Catastrophizing Scale: PCS) [5, 6]. The subjects were divided into three categories according to the PainDETECT scores: the Non-neuropathic pain (NP) group (score of 12 or less; low likelihood of involvement of neuropathic pain), the Suspected NP group (score of 13–18; possible involvement of neuropathic pain), and the NP group (score of 19 or higher; strong suggestion of the involvement of neuropathic pain). The HADS consisted of HADS-anxiety (7 anxiety-related items: HADS-A) and HADS-depression (7 depression-related items: HADS-D). The responders were divided according to the HADS-A and HADS-D scores (21 at the maximum each) into 3 categories: score of 7 or less (no problem), score of 8–10 (possible clinical problems), and score of 11 or higher (evident clinical problems). Responders with HADS-A/D scores of 10 or less (non-anxiety group, non-depression group) and those with HADS-A/D scores of 11 or higher (anxiety group, depression group) were compared. Chronic pain was defined as pain experienced at least once in the past 30 days, with severity of 5 or more on a visual analogue scale (VAS), and persisting for 6 months or more, similar to the definition adopted in the 2010 and 2011 surveys [2, 3]. Furthermore, the age, gender, treatment period, frequency of change of the treating facility, VAS score, PainDETECT score, HADS score and PCS score in the responders with persistent chronic pain were compared among medical facilities and folk remedies. For inter-group comparison, *t* test or ANOVA was used for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. This study was approved by the IRB of Keio University.

Results

Characteristics of the responders complaining of persistent chronic pain

According to the definition of chronic pain, 365 (62 %) of the 588 respondents had persistent chronic pain, while the remaining 223 respondents (38 %) no longer complained of chronic pain. A noteworthy finding was that the most frequently recorded duration of pain was 10–15 years, and the second most frequently recorded duration was 5–10 years (Fig. 1). The most frequently recorded site of pain was the low back (75 %), followed by the neck and shoulder (about 60 %), similar to the results of the previous surveys (Fig. 2a). When individual respondents were questioned about the site of the most persistent pain, the most frequent response was the lower back (33 %), followed by the neck and shoulder (Fig. 2b).

Treatment status among responders complaining of persistent chronic pain

Of the 365 responders complaining of persistent chronic pain, 128 (35 %) were still receiving treatment at the time of the survey, while 193 (53 %) had discontinued treatment. Forty-four responders (12 %) were not receiving treatment despite the presence of persistent pain (Fig. 3a). The treatment period was 1 year or longer in about 40 % of all respondents, indicating a tendency for prolonged treatment (Fig. 3b). When questioned about the outcome of

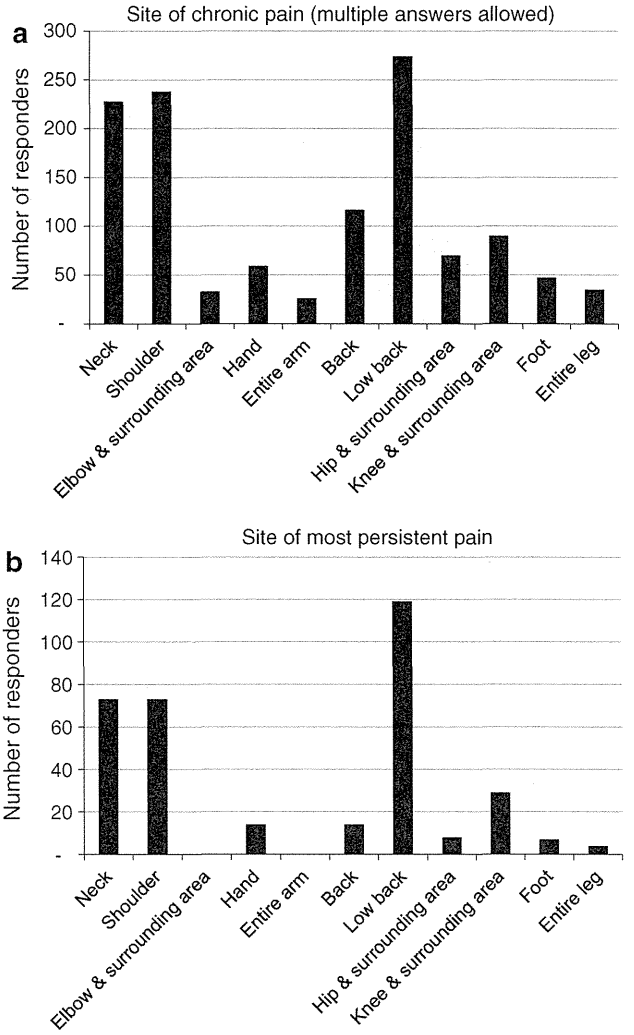

Fig. 2 **a** Site of chronic pain (multiple answers allowed), **b** site of the most persistent pain

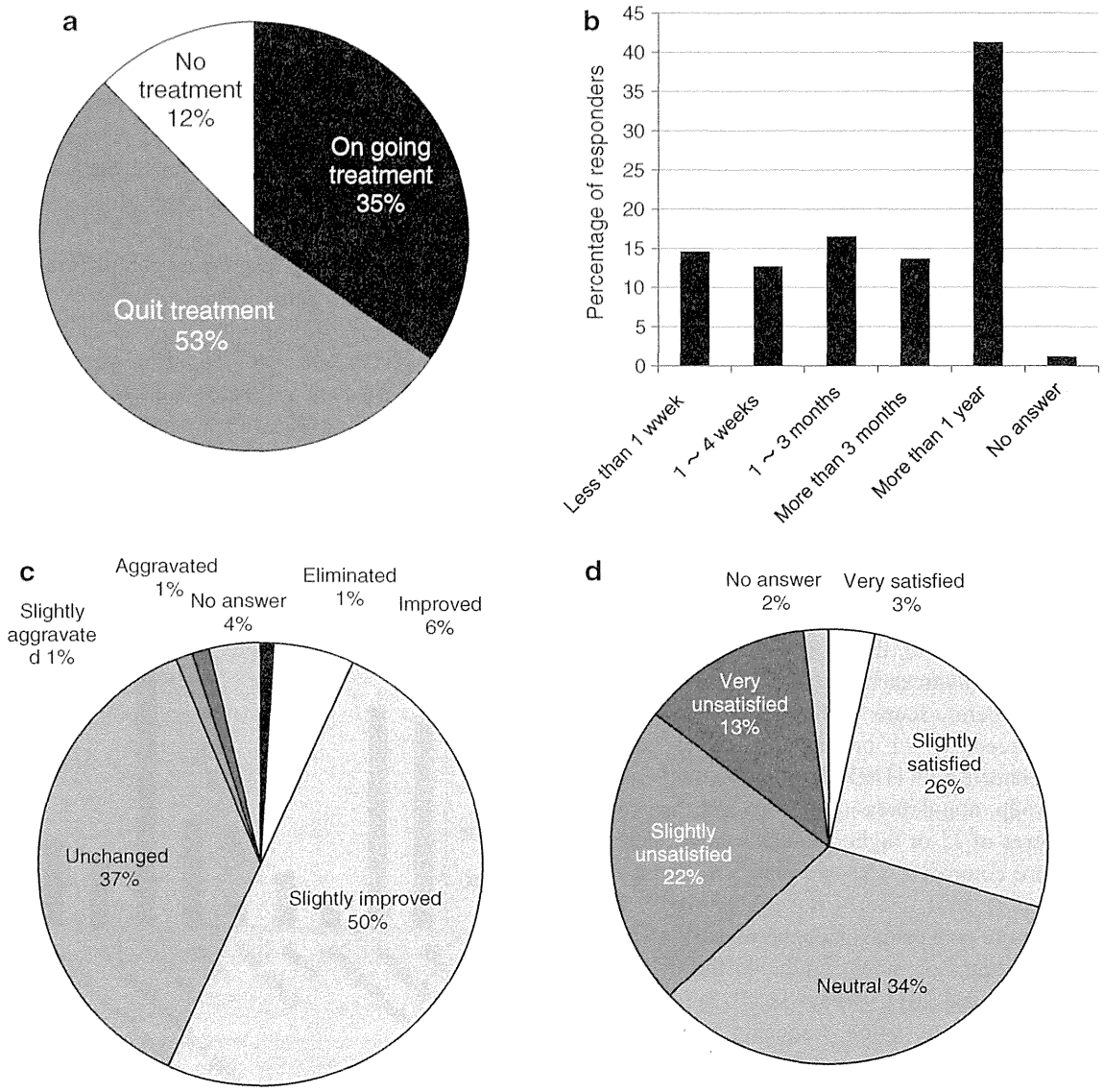

Fig. 3 Treatments received for persistent, chronic pain: **a** treatment circumstances, **b** duration of treatment, **c** efficacy of first treatment, **d** degree of satisfaction with first treatment

treatment at the first treating facility, the responses were "disappeared, improved or slightly improved" in 57 %, and "unchanged, slightly aggravated or aggravated" in 39 % (Fig. 3c). The degree of satisfaction with treatment was "very satisfied or slightly satisfied" in only 29 %, and "neutral, slightly unsatisfied or very unsatisfied" in as many as 69 % of the cases (Fig. 3d).

As a result, the responders often changed the treating facility (66 %), with the frequency of change being once in 40 %, twice in 3 %, three times in 11 %, and 4 times or more in 18 % of the cases (Fig. 4a, b). In a further analysis of the changes in the treating facility, the type of facility providing the initial treatment was most frequently orthopedics (185 responders, 58 %), followed in frequency by a chiropractic/osteopathy (82 responders, 26 %). However, when asked about the type of facility visited as the second treating facility, a smaller number of responders answered "orthopedics" (84 responders) and a larger number of responders answered "chiropractic/osteopathy" (87 responders), with scarce change in the number of responders answering "massage/acupuncture." When asked about the type of facility visited as the third and subsequent treating facility, the number of responses for each type of facility decreased to a similar degree (Fig. 4c).

The most frequent reason for changing the treating facility was "treatment was ineffective" (35 %), followed by "I did not have sufficient time" (30 %), "I thought I could take care of it myself" (10 %), and "it was economically unaffordable" (10 %) (Fig. 5a). The reason for not receiving any treatment was "efficacy was not

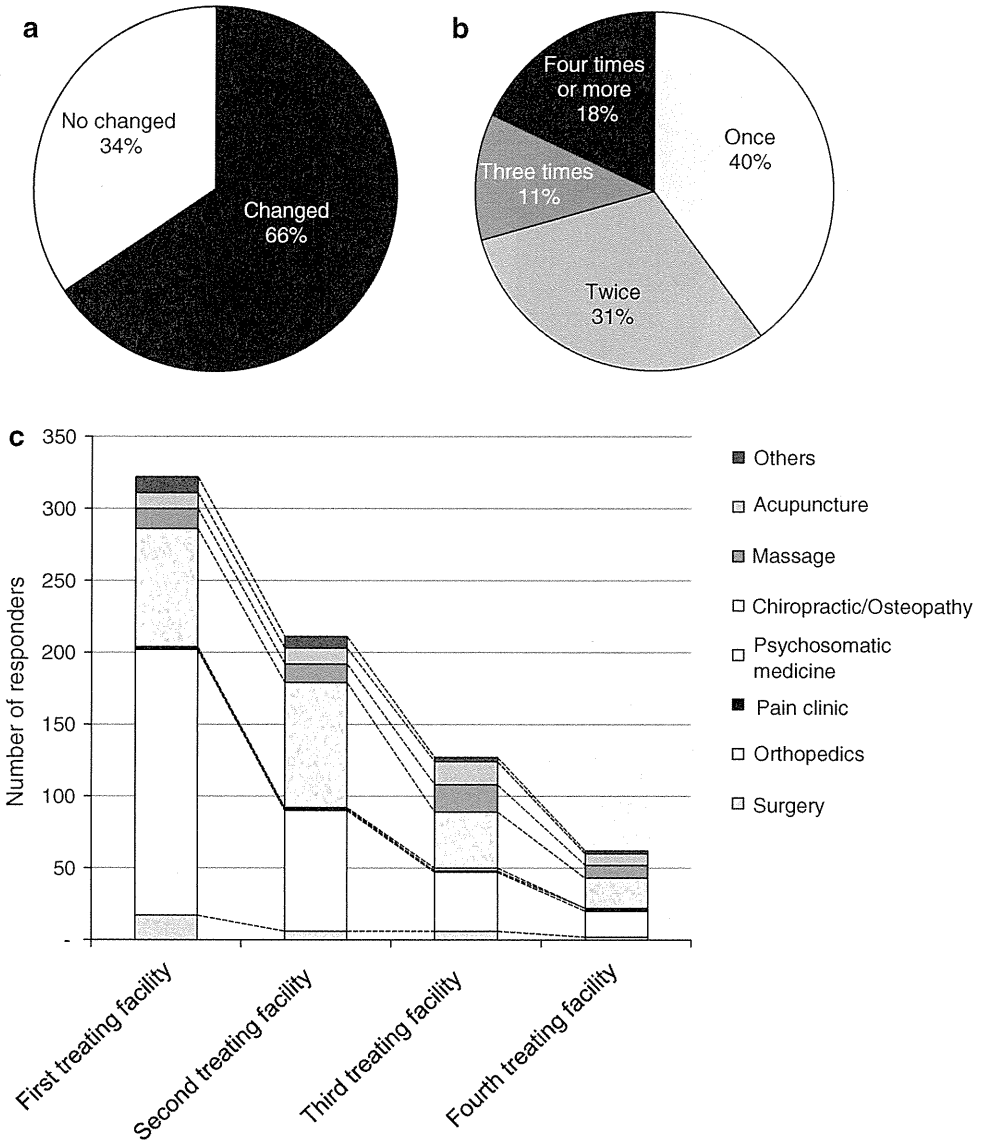

Fig. 4 Circumstances of changes in treatment facility: **a** whether changed, **b** frequency of change, **c** history of change of the treatment facility

expected" (29 %), "I thought it may be possible to deal with the pain by myself" (27 %), "I wanted to receive treatment, but could not receive it" (18 %), and "treatment seemed to be unnecessary" (11 %) (Fig. 5b).

Involvement of neuropathic pain in persistent chronic pain

Involvement of neuropathic pain in the responders complaining of persistent chronic pain was investigated through analysis of the PainDETECT scores. The percentage of responders classified into the NP group was 7 %, and that of responders classified into the Suspect NP group was 13 % (Fig. 6a). In an analysis of the relation to gender, involvement of neuropathic pain was seen more frequently in males than in females with a marginal significance ($p = 0.06$) (Fig. 6b). In the analysis of the relationship between the VAS score and PainDETECT score, the VAS scores differed significantly among the three groups divided according to the involvement of neuropathic pain. There were significant differences in VAS scores between the non-NP and Suspect-NP groups ($p = 0.043$), and between the non-NP and NP groups ($p < 0.001$, Bonferroni post-hoc test) (Fig. 6c). There was a significant difference in the frequency of change of the treating facility among the three groups ($p < 0.05$). Even after removing the influence of VAS score, covariance analysis revealed that the frequency of change of the treating facility was lower in the non-NP group compared to the NP group with a marginal significance ($p = 0.056$) (Fig. 6d).

Involvement of psychogenic pain in persistent chronic pain

The involvement of psychological factors in chronic musculoskeletal pain was investigated through analysis of the correlation between the VAS scores and PCS scores. This

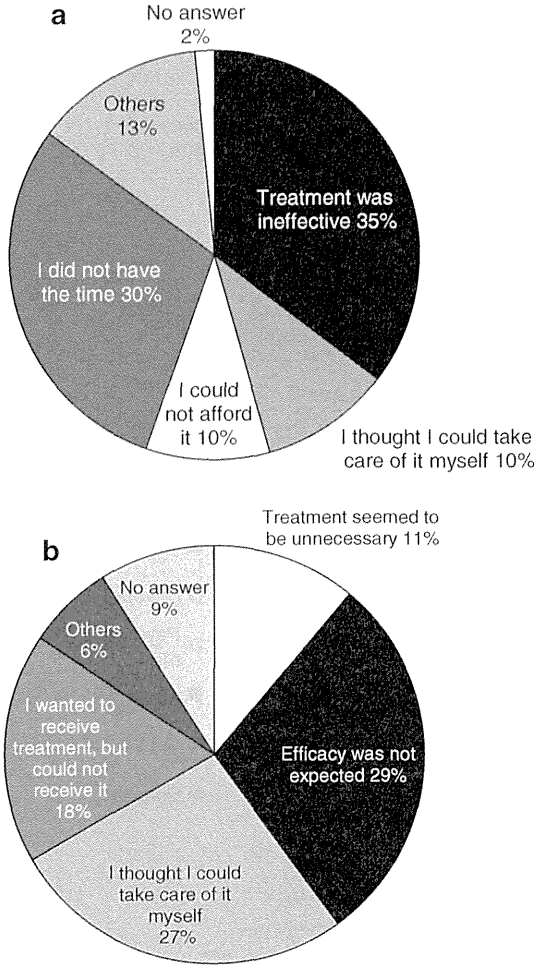

Fig. 5 **a** Reason for discontinuation of treatment, **b** reason for seeking no treatment

analysis revealed a weak but statistically significant positive correlation between the VAS and PCS scores (Spearman's correlation coefficient = 0.224, $p < 0.001$) (Fig. 7a). When analyzed in relation to the HADS-A score, the VAS score was significantly higher in the responders classified into the anxiety group than in the responders classified into the non-anxiety group, while the duration of pain did not differ significantly between the two groups. When analyzed in relation to the HAD-D score, the duration of pain was significantly longer in the depression group than in the non-depression group ($p = 0.019$, covariance analysis with VAS score), while the VAS score did not differ significantly between the two groups (Fig. 7b).

Characteristics of the responders complaining of persistent chronic pain, analyzed by the type of the first treating facility

The characteristics of the responders complaining of persistent chronic pain were compared between the two groups divided by the type of the first treating facility, i.e., the group which received the first treatment at a medical facility (medical facility group) and the group which received the first treatment at a folk remedy (folk remedy group). The male-to-female ratio did not differ significantly between the medical facility group and the folk remedy group, however, the age of the responders was significantly higher in the medical facility group than in the folk remedy group. There was no significant difference in terms of the treatment period or the frequency of change of the treating facility between the two groups. The VAS score did not differ between the two groups either. The PainDETECT score tended to be higher in the medical facility group (8.3) than in the folk remedy group (6.4), although the difference was not statistically significant ($p = 0.06$). The PCS score was significantly higher in the medical facility group (26.5) than in the folk remedy group (23.2) ($p < 0.01$, Table 1).

Discussion

Current status of responders complaining of persistent chronic musculoskeletal pain

Of the responders who complained of chronic musculoskeletal pain at the time of the survey in 2010, 45 % continued to complain of chronic pain in the 2011 survey, and the percentage of responders still complaining of chronic pain rose to 62 % in the survey of 2012. This result suggests that relief from chronic musculoskeletal pain becomes more difficult as the duration of chronic pain increases. In the present survey, the mean VAS score was higher than the score recorded in the 2010 survey, and the most frequent site of pain was the low back (70 %), suggesting the possibility that many of the responders complaining of chronic pain in this survey had intractable low back pain. This finding is consistent with the results of the longitudinal epidemiological survey of 2011, in which the pain in the "low back" as the site of pain and pain for "5 years or longer" as the duration of pain were suggested as risk factors for the persistence of chronic pain [3]. Past reports have also suggested that lower back pain is associated with a high risk of relapse and a chronic course [7–11]. Therefore, approaches for dealing with the high-risk group will become more important when countermeasures against chronic musculoskeletal pain are discussed.

Problems with treatment of persistent chronic pain and countermeasures

Slightly more than 80 % of all responders complaining of persistent chronic pain had a history of treatment, with the treatment still continuing in 30 % of the respondents at the

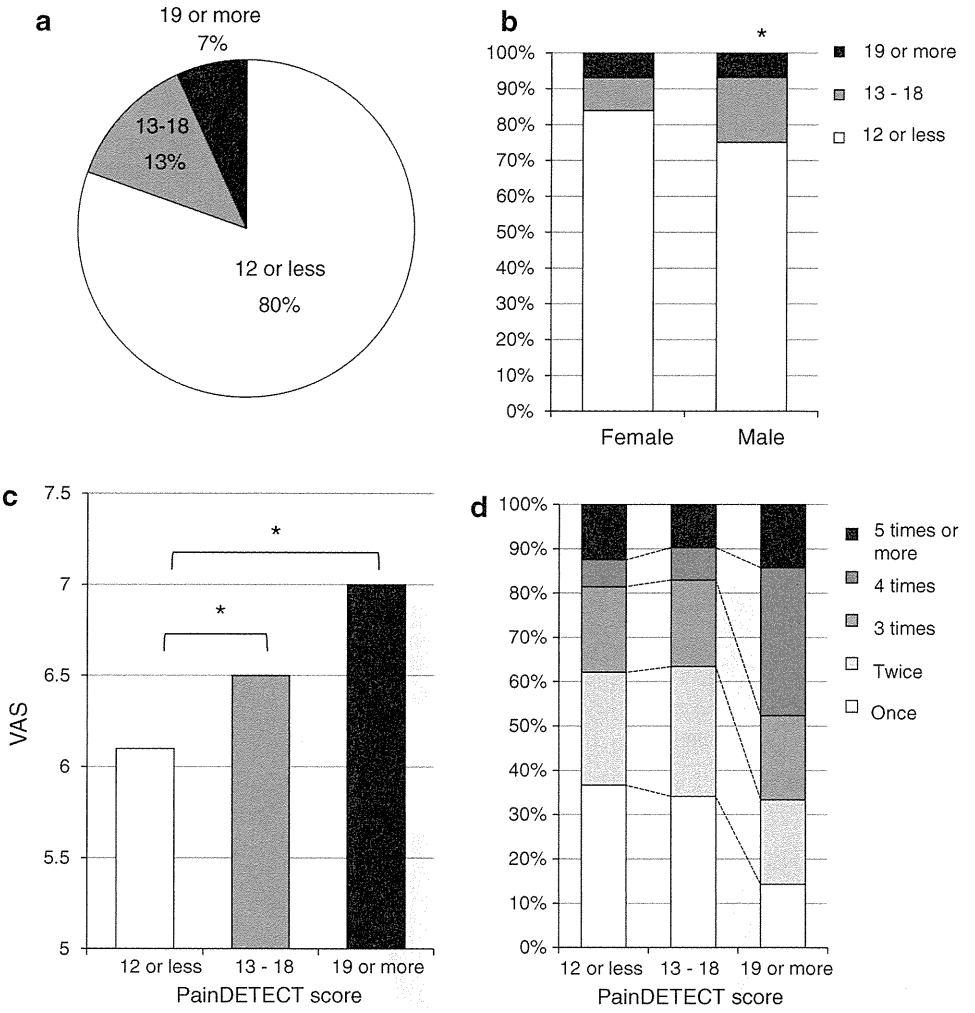

Fig. 6 Influence of neuropathic pain on chronic pain: **a** distribution of the painDETECT scores, **b** comparison of painDETECT scores between males and females (*$p = 0.06$), **c** correlation between painDETECT scores and VAS scores (*$p < 0.05$), **d** influence of painDETECT score on frequency of change of the treatment facility

time of the present survey. The remaining 50 % were no longer receiving treatment despite persistent pain. When asked about the efficacy of treatment, about 40 % answered "unchanged" or "aggravated," with the degree of satisfaction with the treatment being "neutral," "slightly unsatisfied" or "quite unsatisfied" in about 70 %. This tendency was similar to that seen in the 2011 survey. Thus, 66 % of respondents complaining of chronic pain changed the treating facility, with the frequency of change being once or twice in about 70 % of the responders who changed the treating facility. To our surprise, 30 % of the responders changed their treating facility three or more times, suggesting that the percentage of responders engaging in so-called "doctor shopping" cannot be ignored. When changes in the type of the treating facility were analyzed, the first treating facility was an orthopedics in slightly more than 60 % of all responders, while the share of orthopedics as the treating facility decreased to about 50 % after the first change of the treating facility. There was, however, no marked change in the share of folk remedies as the treating facility. This result is consistent with the finding from the survey of 2011, which revealed that the degree of satisfaction with treatment at medical facilities was lower than that at folk remedies [3], suggesting that the initial treatment provided at medical facilities may not be adequate. However, there was no marked difference between medical facilities and folk remedies in terms of the tendency towards subsequent changes of the treating facility. The most frequent reason for changing the treating facility or discontinuing treatment was "treatment was ineffective," indicating that the current approach for treating chronic musculoskeletal pain may not be sufficiently effective. To identify the factors possibly underlying this finding, we investigated the involvement of neuropathic pain and psychogenic pain in persistent chronic musculoskeletal pain.

This analysis suggested possible involvement of neuropathic pain in about 20 % of all responders complaining of chronic pain. It was additionally revealed that the VAS score rose significantly and the frequency of change of the

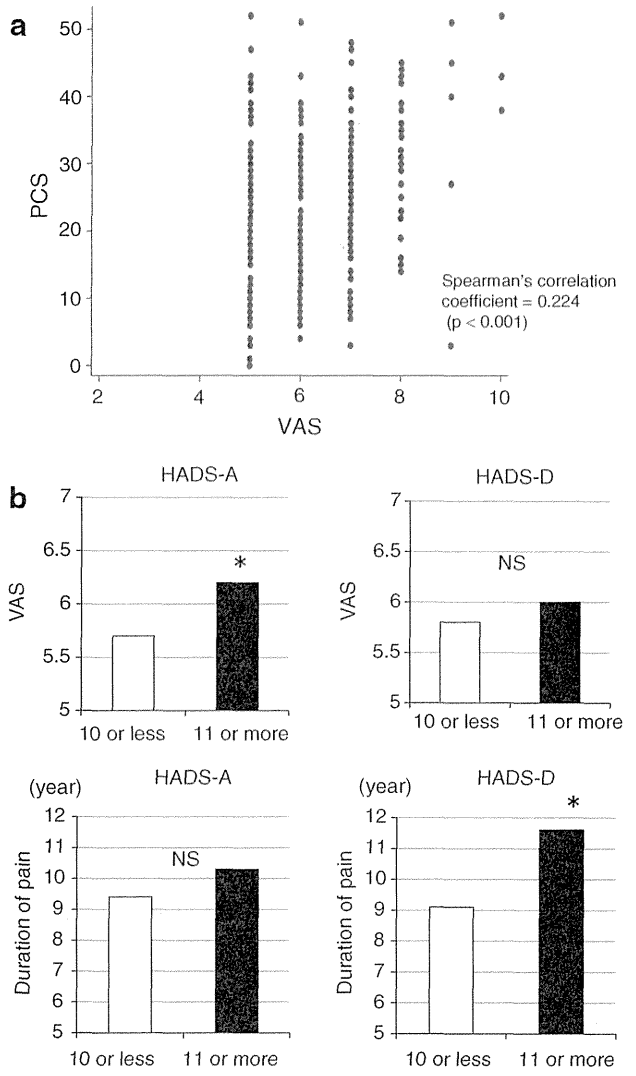

Fig. 7 Influence of psychogenic pain on chronic pain: **a** correlation between PCS and VAS scores, **b** influence of HADS-A (anxiety) and HADS-D (depression) scores on the VAS score and duration of pain (*$p < 0.05$)

Table 1 Characteristics of the responders with chronic pain, analyzed by the type of the first treating facility

		Medical facility ($n = 213$)	Folk remedy ($n = 108$)	p value*
Sex				
Female	Number (column %)	129 (60.3)	75 (69.4)	0.11
Male		85 (39.7)	33 (30.6)	
Age	Average (SD)	54.8 (14.8)	46.2 (13.8)	<0.01
Duration of treatment (years)	Average (SD)	10.3(9.0)	10.4 (7.2)	0.91
Frequency of change in the treatment facility	Number (column %)			
1		77 (36.0)	34 (31.5)	0.65
2		51 (23.8)	33 (30.6)	
3		43 (20.1)	22 (20.4)	
4		18 (8.4)	6 (5.6)	
5 or more		25 (11.7)	13 (12.0)	
VAS	Average (SD)	6.1 (1.1)	6.4 (1.1)	0.13
PainDETECT score	Average (SD)	8.3 (6.7)	6.8 (5.9)	0.06
PainDETECT				
12 or less	Number (column %)	146 (76.4)	86 (83.5)	0.34
13–18		29 (15.2)	12 (11.7)	
19 or more		16 (8.4)	5 (4.9)	
PCS score	Average (SD)	26.5 (10.3)	23.2 (9.9)	<0.01

* t test, χ^2 test, Fisher's exact

treating facility also increased as the likelihood of involvement of neuropathic pain became higher. Regarding psychogenic pain, a significant positive correlation was noted between PCS and VAS scores, an increase in HADS-A score was associated with an increase of the VAS score, and an increase in the HADS-D score was associated with a longer duration of pain. In regard to chronic low back pain, which was the most frequent type of pain recorded in the present survey, the previously reported important role of psychogenic factors [12–16] was also endorsed by the results of the present survey. Interestingly enough, analysis of the characteristics of the responders complaining of chronic pain in relation to the type of the first treating facility revealed that medical facilities more frequently managed patients of advanced age and with a stronger likelihood of involvement of neuropathic pain and psychogenic pain than folk remedies. These factors may explain, at least partially, the relatively low satisfaction level of responders with the treatment at medical facilities. However, caution is needed while interpreting the results as to psychogenic pain, in view of the possibility that treatment may result in progression of catastrophic thinking or depressive mood.

Taken together, these results suggest that many of the patients complaining of chronic musculoskeletal pain seek treatment at the orthopedic clinic/department first, but tend to show low levels of satisfaction with the treatment because of insufficient efficacy, and that neuropathic pain and psychogenic pain may be involved in the poor responses of these patients to treatment. Lack of adequate assessment for neuropathic and psychogenic pain during the initial treatment of chronic

musculoskeletal pain and the resultant absence of appropriate treatment seem to lead to "doctor shopping" by patients. A past report also pointed out the close involvement of neuropathic pain with chronic low back pain [17]. To resolve this issue, it will be important to assess the involvement of neuropathic pain on the basis of the PainDETECT score and neuropathic severity score before treatment is started in individual patients complaining of chronic musculoskeletal pain. Furthermore, the results of the present survey suggest that if treatment is provided in a manner tailored to the status of involvement of psychogenic pain rated by the HADS and PCS, it may become possible to reduce the intensity of pain and shorten the duration of pain.

Many previous reports have shown that chronic musculoskeletal pain can impair not only physical health, but also mental health, which may have a large impact on the daily living and social activities of the patients [2, 18]. However, the awareness among patients about chronic pain does not seem to be sufficient, considering the finding from this survey that patients often decided to discontinue treatment or seek no treatment for chronic pain persisting for 3 years or more, on grounds such as "I did not have sufficient time," "I thought I could take care of it myself" and "I thought treatment was unnecessary." At present, the actual status of chronic musculoskeletal pain is not sufficiently well understood by the people in Japan. Dissemination of information through various media to deepen the understanding of the people is important for ensuring a sufficient level of awareness among the people of Japan about the significance of chronic musculoskeletal pain treatment.

This study was conducted as a 2011 Ministry of Health, Labour and Welfare: Health Labour Sciences Research Grant for Comprehensive Research on Disability Health and Welfare (Survey study of chronic musculoskeletal pain).

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Conflict of interest The authors declare that they have no conflict of interest.

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Suzuki et al. Journal of Intensive Care 2014, 2:5
http://www.jintensivecare.com/content/2/1/5

JOURNAL OF INTENSIVE CARE

RESEARCH Open Access

Evaluation of noninvasive positive pressure ventilation after extubation from moderate positive end-expiratory pressure level in patients undergoing cardiovascular surgery: a prospective observational study

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Abstract

Background: It remains to be clarified if the application of noninvasive positive pressure ventilation (NPPV) is effective after extubation in patients with hypoxemic respiratory failure who require the sufficient level of positive end-expiratory pressure (PEEP). This study was aimed at examining the effect and the safety of NPPV application following extubation in patients requiring moderate PEEP level for sufficient oxygenation after cardiovascular surgery.

Methods: With institutional ethic committee approval, the patients ventilated invasively for over 48 h after cardiovascular surgery were enrolled in this study. The patients who failed the first spontaneous breathing trial (SBT) at 5 cmH_2O of PEEP, but passed the second SBT at 8 cmH_2O of PEEP, received NPPV immediately after extubation following our weaning protocol. Respiratory parameters (partial pressure of arterial oxygen tension to inspiratory oxygen fraction ratio: P/F ratio, respiratory ratio, and partial pressure of arterial carbon dioxide: $PaCO_2$) 2 h after extubation were evaluated with those just before extubation as the primary outcome. The rate of re-intubation, the frequency of respiratory failure and intolerance of NPPV, the duration of NPPV, and the length of intensive care unit (ICU) stay were also recorded.

Results: While 51 postcardiovascular surgery patients were screened, 6 patients who met the criteria received NPPV after extubation. P/F ratio was increased significantly after extubation compared with that before extubation (325 ± 85 versus 245 ± 55 mmHg, $p < 0.05$). The other respiratory parameters did not change significantly. Re-intubation, respiratory failure, and intolerance of NPPV never occurred. The duration of NPPV and the length of ICU stay were 2.7 ± 0.7 (SD) and 7.5 (6 to 10) (interquartile range) days, respectively.

Conclusions: While further investigation should be warranted, NPPV could be applied effectively and safely after extubation in patients requiring the moderate PEEP level after cardiovascular surgery.

Keywords: Weaning, Invasive mechanical ventilation, Noninvasive positive pressure ventilation, Moderate PEEP level, Cardiovascular surgery

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Background

Prolonged invasive mechanical ventilation (IMV) through endotracheal tube, appreciated as the most efficient way to provide sufficient oxygenation in patients with respiratory failure, is ironically likely to cause various complications such as ventilator-induced lung injury and ventilator-associated pneumonia, leading to an increase of mortality [1,2]. Thus, one of the major goals in the intensive care unit (ICU) is to wean critical ill patients from such IMV as early as possible without consequent respiratory failure and re-intubation. A number of clinical trials have demonstrated that the clinical strategy such as daily interruption of sedation [3], protocol-based sedation [4], and awaking and breathing trial [5] to obviate the prolonged duration of IMV is beneficial.

Previous studies showed that noninvasive positive pressure ventilation (NPPV) is safe and effective to facilitate weaning from IMV in especially medical patients requiring long-term ventilatory support for predominantly hypercapnic respiratory failure [6-8]. However, there are few data which describe the effectiveness of NPPV to facilitate the process of liberation from IMV in patients with hypoxemic respiratory failure. Due to severe postoperative pulmonary complications such as atelectasis, pulmonary edema, pneumonia, and phrenic nerve palsy, postcardiovascular surgery patients often develop hypoxemic respiratory failure requiring high level of positive end-expiratory pressure (PEEP) for sufficient oxygenation and could suffer from prolonged IMV [9,10]. Although NPPV has been used widely for postoperative respiratory failure [11,12], there are few studies to examine whether NPPV can be applied effectively and safely after extubation in such population who requires sufficient PEEP level and long-term ventilator support after cardiovascular surgery.

We, therefore, designed the present study to evaluate the effect and the safety of our weaning protocol in which NPPV was applied after extubation in these patients who were mechanically ventilated for over 48 h and simultaneously required moderate PEEP level for sufficient oxygenation after cardiovascular surgery.

Methods

We conducted this prospective observational study in our eight-bed ICU of Kawasaki Municipal Hospital in Japan. Institutional review board approval was obtained and thereby allowed us to wave the need of informed consent since this is an observational study and the application of NPPV after extubation is performed in a routine manner in our ICU.

Study protocol

Patients who underwent cardiovascular surgery from April 2011 to December 2011 in our hospital were screened. All patients who received mechanical ventilation via endotracheal tube for over 48 h after cardiovascular surgery were enrolled in this study. Exclusion criteria were younger than 20 years old, body mass index over 35, and chronic renal failure requiring hemodialysis. We excluded patients on hemodialysis since extubation from moderate PEEP level through NPPV application might be hazardous due to the impracticality of constant diuresis in these patients. Additionally, the patients who could not be weaned from IMV or died within 14 postoperative days (POD) were excluded from the study. Eligible patients were screened every morning and considered ready for weaning if they met all the following weaning criteria: (1) hemodynamic stability requiring less than 3 μg/kg/min of dopamine or dobutamine and/or less than 0.02 μg/kg/min of norepinephrine, (2) partial pressure of arterial oxygen tension to inspiratory oxygen fraction ratio (P/F ratio) more than or equal to 200 mmHg with PEEP of 10 cmH_2O or less, (3) adequate conscious level and cough reflex, and (4) absence of hyperthermia (>38°C) or suspected pneumonia. Pneumonia was suspected in patients with a new or worsened pulmonary infiltrate on chest X-ray who meets any two of the following three criteria: leukocyte count above 12,000 or below 4,000/μL, body temperature above 38°C and/or the presence of purulent respiratory secretions. Patients who met all these weaning criteria were initiated to wean from IMV following our protocol (Figure 1). This protocol was quite different from the conventional one in which the trachea was extubated only after successful spontaneous breathing trial (SBT) at 5 cmH_2O of PEEP.

The first SBT was performed under continuous positive airway pressure (CPAP) mode with pressure support (PS) for 2 h at the following setting: PEEP equal to 5 cmH_2O, PS equal to 5 cmH_2O, and inspiratory oxygen fraction (FIO_2) equal to or less than 0.5. If the patients could tolerate the first SBT in accordance with our extubation criteria described below, the trachea was extubated. The extubation criteria were as follows: (1) P/F ratio ≧200 mmHg, (2) respiratory ratio <30/min, (3) rapid shallow breathing index (the ratio of respiratory frequency to tidal volume) <105, (4) variability of blood pressure and heart rate <20%, (5) adequate conscious level and cough reflex, and (6) no agitation. If the first SBT failed, the second SBT was performed for 2 h at the following setting immediately after the first SBT followed by recruitment maneuver (30 cmH_2O for 30 s) application, CPAP mode with PEEP equal to 8 cmH_2O, PS equal to 5 cmH_2O, and FIO_2 equal to or less than 0.5. If the extubation criteria during the second SBT were confirmed, they received sequential NPPV (BiPAP vision, Respironics, Murrysvile, PA, USA) through a full facial mask immediately after extubation. NPPV was delivered at the CPAP mode with 8 cmH_2O of PEEP and the same FIO_2 as before extubation. During NPPV, all patients were

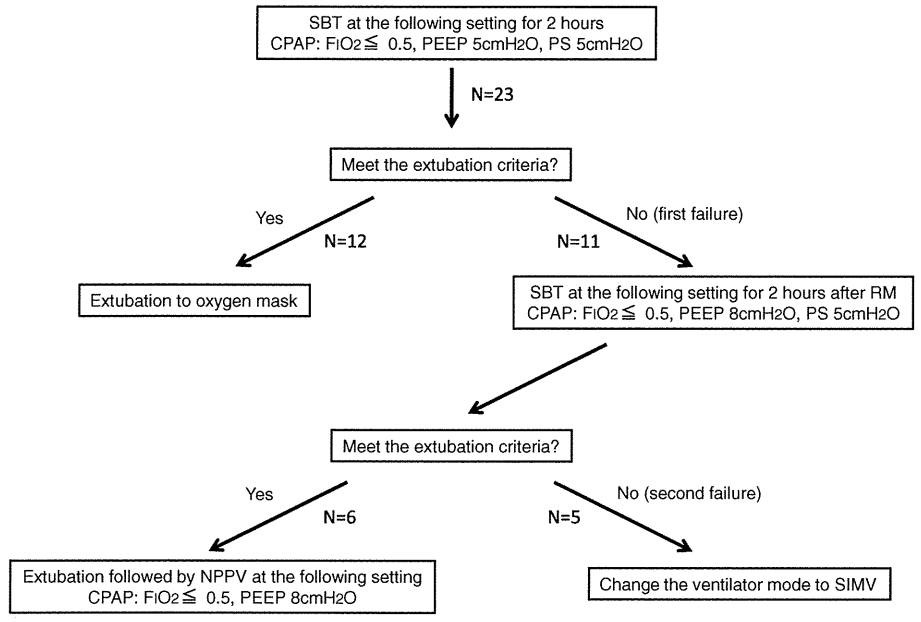

Figure 1 Study protocol for weaning from invasive ventilator support. SBT, spontaneous breathing trial; CPAP, continuous positive airway pressure; FIO_2, inspiratory oxygen fraction; PEEP, positive end-expiratory pressure; PS, pressure support; RM, recruitment maneuver, RM was performed at the pressure of 30 cmH_2O for 30 s; SIMV, synchronized intermittent mandatory ventilation.

administered an infusion of dexmedetomidine (0.2 to 0.7 μg/kg/hr) to relieve discomfort. Ventilator setting was not changed for 2 h if O_2 saturation monitored by pulse oximetry (SpO_2) was maintained more than 92% and respiratory rate was less than 35 breaths/min. At 2 h after extubation, the setting was adjusted to achieve SpO_2 >94% and respiratory rate <30 breaths/min if necessary. The physicians in charge were allowed to use S/T mode with different inspiratory and expiratory positive pressure at any time if indicated. NPPV was applied at least for 12 h and weaned by reducing positive pressure level gradually by 2 cmH_2O while maintaining SpO_2 >94% and respiratory rate <30 breaths/min. Since the reason why these patients require moderate PEEP for sufficient oxygenation should be overhydration, we dehydrated these patients using diuretics to wean from NPPV while paying strict attentions to hemodynamic stability. Once the PEEP level of 4cmH_2O and FIO_2 equal to or less than 0.5 were achieved, arterial blood gases were analyzed 2 h later. If P/F ratio was above 200 mmHg, patients were weaned from NPPV and received O_2 mask (total flow, 30 L/min; FIO_2, 0.5). Weaning from NPPV was considered as successful unless respiratory failure developed for 24 h after liberation from NPPV, defined as the presence of any of the following criteria: (1) severe hypoxemia with SpO_2 <92% or PaO_2 <70 mmHg at FIO_2 of 0.5 or more, (2) respiratory rate >35 breaths/min, (3) respiratory acidosis (arterial pH <7.3 with a partial pressure of arterial carbon dioxide ($PaCO_2$) >50 mmHg), (4) clinical signs of respiratory muscle fatigue such as use of accessory muscle and paradoxical motion of the abdomen, (5) inability to remove tracheal secretions, or (6) severe dyspnea.

Criteria for re-intubation

Patients were immediately intubated if any of the following criteria was unmasked: (1) respiratory or cardiac arrest, (2) respiratory pauses with loss of consciousness or gasping, (3) uncontrolled agitation, (4) massive aspiration, (5) the inability to remove respiratory secretions, or (6) hemodynamic instability unresolved by fluids and vasoactive agents. Furthermore, the patients were re-intubated if respiratory failure described above persisted for over 4 h despite adjustment of ventilator setting and possible medical or physical therapy.

Measurement parameters

At baseline, demographic data, SOFA score at ICU admission, diagnosis for surgery, and duration of IMV before extubation were recorded. Arterial pressure, heart rate, respiratory rate, and SpO_2 were monitored continuously, whereas arterial blood gases were analyzed at 7 a.m. every morning, just before extubation, 2 h after initiation of NPPV and any time if indicated. The duration of NPPV, the presence of re-intubation or respiratory failure, and the length of ICU stay were also recorded. The primary end-point was the changes of respiratory parameters including P/F ratio, respiratory rate, and $PaCO_2$, 2 h after initiation of NPPV compared with those just before extubation. The secondary end-points were the changes of

hemodynamic parameters (systolic blood pressure and heart rate) after initiation of NPPV, the rate of re-intubation, the frequency of respiratory failure and intolerance of NPPV, the duration of NPPV, and the length of ICU stay.

Statistical analysis

Continuous variables were presented as means ± standard deviation (SD), or medians and interquartile ranges, and compared by Student's t test for variables with a normal distribution and by Mann–Whitney U test for variables with a non-normal distribution. Categorial valuables were compared by Fisher's exact probability test. A p value of <0.05 was considered as statistically significant.

Results

Fifty-one patients underwent cardiovascular surgery during the study period. Among them, 27 patients were weaned from IMV within 48 h after surgery, whereas the rest were screened for the eligibility of this study. One patient was excluded from the study because of chronic renal failure requiring hemodialysis. Of another 23 patients, 12 patients were weaned from IMV to face mask in accordance with the weaning protocol of our institute after the first SBT at 5 cmH_2O PEEP (Figure 1), of whom 3 patients were re-intubated and 2 of them underwent tracheostomy at 15 and 16 POD. Among other 11 patients, 5 patients did not meet the extubation criteria (second failure). Namely, two patients had tracheostomy at 15 and 21 POD, one patient died at 10 POD due to acute myocardial infarction, and two patients died at 13 and 18 POD due to multiple organ failure with severe sepsis before extubation. After all, six eligible patients who met the extubation criteria after the second SBT were enrolled for this trial. Clinical characteristics of these patients are summarized in Table 1. Before the successful second SBT, five of six patients failed the first SBT because of hypoxemia (P/F ratio <200 mmHg) and another one patient progressed to tachypnea (respiratory rate ≧30 breaths/min).

In all six patients, NPPV was performed successfully over 12 h without adjusting ventilator setting. The changes of respiratory parameters are described in Table 2. The P/F ratio increased significantly 2 h after initiation of NPPV compared with just before extubation (325 ± 85 mmHg versus 245 ± 55 mmHg, $p < 0.05$), while respiratory rate and $PaCO_2$ did not change significantly (17 ± 5.5/min versus 18.2 ± 6.5/min and 33.2 ± 5.3 mmHg versus 34.0 ± 5.1 mmHg, respectively). Hemodynamic parameters including systolic blood pressure and heart rate did not change significantly after initiation of NPPV compared with those before extubation (Table 3). No patients needed re-intubation or developed respiratory failure after application of NPPV. All patients tolerated the whole NPPV procedure. The duration of NPPV was 2.7 ± 0.7 days, and the length of ICU stay was 7.5 (6 to 10) days. However, the rate of re-intubation and the length of ICU stay of these six patients did not reach statistically significant difference compared with those of 12 patients who were extubated to oxygen face mask more than 48 h after surgeries at low PEEP level of 5 cmH_2O (0/6 versus 3/12; $p = 0.515$, 7.5 (6 to 10) versus 5.5 (4.5 to 8.5) days; $p = 0.256$). All six patients were discharged from the hospital without any severe consequences.

Discussion

The present study showed that an application of NPPV after extubation is safe and effective in patients requiring moderate level of PEEP after cardiovascular surgery. In particular, P/F ratio at 2 h after induction of NPPV improved significantly rather than before extubation. Furthermore, all patients weaned from NPPV successfully without the need of re-intubation and the development of respiratory failure.

NPPV has been used widely now not only in ICU but also in general wards [13], and the efficacy of this technique has been reported in various clinical situations, such as exacerbation of chronic obstructive pulmonary disease (COPD) [14], cardiac pulmonary edema [15], and postoperative respiratory failure [11,12]. Although some previous

Table 1 Characteristics of six patients weaned from invasive mechanical ventilation through application of NPPV

No.	Age	Sex	Height (cm)	Weight (kg)	Diagnosis	Operative procedure	Operation time (h and min)	SOFA score	Duration of IMV (day)	Reason for first failure	Duration of NPPV (day)
1	55	F	161	66	MR, TR	MVR, TAP	7 h and 04 min	8	8	P/F ratio <200 mmHg	2
2	72	M	166	66	Atrial fibrillation	Maze operation	6 h and 00 min	8	3	P/F ratio <200 mmHg	2
3	79	F	148	57	Angina	CABG	5 h and 47 min	7	4	P/F ratio <200 mmHg	4
4	71	M	161	52	Angina	CABG	6 h and 48 min	8	6	RR ≧30/min	2
5	63	M	170	59	Stenosis of right outflow tract	Plasty of right outflow tract	9 h and 47 min	11	8	P/F ratio <200 mmHg	3
6	85	M	160	58	Angina	CABG	3 h and 17 min	5	3	P/F ratio <200 mmHg	3

NPPV, non-invasive positive pressure ventilation; SOFA score, sequential organ failure assessment score; IMV, invasive mechanical ventilation; P/F ratio, partial pressure of arterial oxygen tension to inspiratory oxygen fraction ratio; RR, respiratory ratio; M, male; F, female; MR, mitral regurgitation; TR, tricuspid regurgitation; MVR, mitral valve replacement; TAP, tricuspid annuloplasty; CABG, coronary artery bypass grafting.

Table 2 The changes of respiratory parameters in six eligible patients before and after NPPV application

No.	P/F ratio (mmHg)		RR (/min)		$PaCO_2$ (mmHg)	
	Before	After	Before	After	Before	After
1	201.2	287.4	15	12	32.6	33.0
2	248.3	280.4	13	11	33.3	36.5
3	246.4	298.2	16	14	36.7	28.9
4	351.2	458.4	31	25	34.1	34.7
5	206.6	228.6	18	20	41.3	40.6
6	219.2	398	16	20	25.8	25.7
mean ± SD	245 ± 55	325 ± 85*	18.2 ± 6.5	17.0 ± 5.5	34.0 ± 5.1	33.2 ± 5.3

*$p < 0.05$ compared with before. P/F ratio, partial pressure of arterial oxygen tension to inspiratory oxygen fraction ratio; RR, respiratory ratio; $PaCO_2$, partial pressure of arterial carbon dioxide.

studies examined the effect of NPPV to facilitate a weaning from IMV in patients who required long-term ventilator support and suffered from persistent weaning failure [6-8], our study is quite different from these previous studies in some points. Contrary to previous studies which included medial ICU patients with predominantly hypercapnic COPD patients, our study targeted only patients who have risk factors for developing hypoxemic respiratory failure after cardiovascular surgery. Besides, we applied NPPV after extubation in patients who could maintain sufficient oxygenation at PEEP level of 8 cmH_2O but failed at 5 cmH_2O PEEP following our weaning protocol in this study. We guessed that the major reasons why these six patients required moderate PEEP level were atelectasis, overhydration, and cardiogenic pulmonary edema due to the long procedure of cardiac surgery and large amount of transfusion required for perioperative hemodynamic stability. Thus, it is unclear whether this weaning technique can be generalized to other type of hypoxemic respiratory failure patients. However, one recent small randomized controlled study, including 20 patients, demonstrated that NPPV application after early extubation from moderate level of PEEP was beneficial in non-surgical patients with resolving hypoxemic respiratory failure [16]. Furthermore, early application of nasal CPAP after extubation from 7 cm H_2O PEEP was reported to reduce pulmonary morbidity and length of hospital stay following the surgical repair of thoracoabdominal aortic aneurysms [17]. Thus, weaning strategy through NPPV for patients requiring moderate level of PEEP might be beneficial in wide range of hypoxemic respiratory failure, which should be confirmed by a large randomized controlled trial.

Table 3 The changes of hemodynamic parameters in six eligible patients before and after NPPV application

No.	Systolic BP (mmHg)		HR (beats/min)	
	Before	After	Before	After
1	122	113	89	78
2	145	135	94	87
3	112	121	79	85
4	108	102	82	78
5	138	136	61	65
6	142	128	71	62
mean ± SD	128 ± 16	123 ± 13	79 ± 12	76 ± 10

NPPV, noninvasive positive pressure ventilation; BP, blood pressure; HR, heart rate.

Oxygenation improved significantly after the initiation of NPPV compared with before extubation even though the applied PEEP level was the same (8 cmH_2O). While the exact mechanisms for this improvement is unknown, some possible mechanisms are considered, such as absence of sedation other than dexmedetomidine, increased patient's activity, and improvement of dorsal ventilation leading to reduced V/Q mismatch. Although this improvement of oxygenation could support the use of this weaning strategy, there are some concerns to apply this technique. Delayed intubation after developing respiratory failure is associated with worse outcome [18,19], thereby re-intubation should not be hesitated if respiratory failure once develops. The protocol to prevent delayed re-intubation should be made in all ICU where patients with respiratory failure are treated by NPPV. Tolerance of patients is also one of the key factors in managing NPPV successfully. Although patients were sedated with remifentanil or propofol to increase NPPV tolerance in previous studies [20,21], we used continuous dexmedetomidine infusion, which has little respiratory depressant effects, to relieve discomfort as a routine practice, probably contributing to the high successful rate of NPPV management in our ICU.

There are several limitations to interpret the data herein. *First*, this study is not a randomized controlled trial but an observational study, and the sample size was too small. It remains unknown whether this technique can reduce the length of mechanical ventilation, the rate of complication relating to IMV, the length of ICU stay, and the mortality compared with the conventional weaning strategy. However, all 6 patients enrolled in this study could wean from IMV through application of NPPV without any progression

to respiratory failure and the need of re-intubation, while 3 of 12 patients who were liberated from IMV to oxygen face mask were re-intubated even though they passed SBT at the low PEEP level (5 cmH_2O). Although the rate of re-intubation did not reach significant difference, this might be attributed to the small sample size. Whether this weaning strategy could reduce the rate of re-intubation, it should be evaluated in a randomized controlled trial in the future. *Second*, we performed two sequential SBT for 4 h in this study protocol which could be too long procedure, while some weaning guideline recommends SBT should be performed every 24 h [22]. However, there are no evidences as to the appropriate duration of SBT. *Finally*, there is no rationale for 8 cm H_2O of PEEP level at which trachea were extubated in this study. It may be plausible that patients could be liberated from IMV at higher level of PEEP, which should be examined in a future study.

Conclusions

Application of NPPV after liberation from IMV via tracheal intubation was safe and effective in patients who required moderate level of PEEP for sufficient oxygenation after cardiovascular surgery. The P/F ratio improved significantly 2 h after initiation of NPPV compared with that just before extubation, and all patients could wean successfully without development of respiratory failure and re-intubation. A randomized controlled trial is warranted to confirm the effectiveness of this technique before it is widely used in other ICU.

Abbreviations

COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure; FIO_2: inspiratory oxygen fraction; ICU: intensive care unit; IMV: invasive mechanical ventilation; NPPV: noninvasive positive pressure ventilation; P/F ratio: PaO_2 to FIO_2 ratio; $PaCO_2$: partial pressure of arterial carbon dioxide; PaO_2: partial pressure of arterial oxygen tension; PEEP: positive end-expiratory pressure; PS: pressure support; SBT: spontaneous breathing trial; SD: standard deviation; SOFA score: sequential organ failure assessment score; SpO_2: O_2 saturation monitored by pulse oximetry.

Competing interests

The authors declare that they have no competing interest.

Authors' contributions

TS planned and conducted the study, collected the data, and drafted the manuscript. TK, ST, YM, and YM participated in planning the study design, conducted the study, and helped in drafting the manuscript. JM gave advice for planning the study, coordinated all the study, and helped in drafting the manuscript. SK and NK participated in planning the study design, analyzed the data, and helped in drafting the manuscript. HM helped to coordinate the study, and supervised all parts of the study. All authors read and approved the final manuscript.

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Received: 11 August 2013 Accepted: 8 January 2014
Published: 23 January 2014

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doi:10.1186/2052-0492-2-5
Cite this article as: Suzuki *et al.*: Evaluation of noninvasive positive pressure ventilation after extubation from moderate positive end-expiratory pressure level in patients undergoing cardiovascular surgery: a prospective observational study. *Journal of Intensive Care* 2014 2:5.