

multicenter trial with a fixed standard protocol was considered essential for establishing solid evidence that confirms the clinical significance of SN mapping in gastric cancer. A study group of the Japan Society of Sentinel Node Navigation Surgery analyzed the results of the previous studies and formulated an optimal procedure for SN mapping using the dual tracer method with technetium 99m-labeled tin colloid and 1% isosulfan blue dye (Lymphazurin, TycoHealth Care, Tokyo, Japan) in which the detection rate and sensitivity to detect metastasis by SN biopsy was relatively high.^{5,10} Twelve institutions with established SN mapping protocols in place and experienced surgical staffs participated in this prospective study in which the validity of the SN concept and current optimal indications and procedures for gastric cancer treatment were evaluated.

PATIENTS AND METHODS

Patients

Patients with histologically confirmed clinical T1N0M0 or T2N0M0 adenocarcinoma of the stomach (International Union Against Cancer [UICC] TNM Classification, 6th edition) with single primary lesions (≤ 4 cm) without previous treatment, including endoscopic mucosal resection or endoscopic submucosal dissection, were preoperatively considered for inclusion in this study. Clinical staging was made by preoperative endoscopy and computed tomography. Endoscopic ultrasound was not routinely performed in the patients included in this study. Patients with apparent T3/T4 tumors, nodal or distant metastasis diagnosed intraoperatively, extensive abdominal adhesion, or poor general condition during surgery were excluded from the study. Patients with a history of drug-related allergy or active asthma were also excluded because of the potential risk of anaphylactic reaction after blue dye injection. All patients enrolled onto this study were preoperatively registered in a central data center.

All patients provided written informed consent. This study was approved by all local institutional review boards and conducted in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki. The 12 hospitals that participated in this multicenter prospective study had previous experience (> 30 patients each) with SN mapping for gastric cancer using the dual tracer method.

SN Mapping Procedure

The dual tracer method with radiolabeled tin colloid and blue dye was performed as previously described.⁵ Briefly, the day before surgery, 20 mL of technetium 99m tin colloid solution (0.5 mL \times 4 points; total 150 MBq; 0.3 mCi at the time of surgery) was injected in four quadrants of the submucosal layer of the primary lesion by using an endoscopic puncture needle. Intraoperatively, the gastrocolic ligament was divided to visualize all possible directions of lymphatic flow from the stomach. The 1% isosulfan blue dye was injected via intraoperative endoscopy in exactly the same manner as the preoperative injection of the radioactive tracer. Within 15 minutes, the lymphatic vessels and lymph nodes were dyed blue and imaged. Simultaneously, a hand-held gamma probe was used to locate the radioactive SN. Lymph nodes with radioactivity $> 10\times$ background activity were defined as hot nodes. Hot and/or blue nodes were identified as the SNs in this study. In principle, the dual tracer technique was performed as an ideal SN mapping procedure in this study. However, the radioguided method alone was also permitted per our protocol in cases in which it was difficult to intraoperatively inject the blue dye.

Intraoperative Histologic Examination of SNs

Harvested SNs were subjected to intraoperative histologic examination by hematoxylin and eosin (HE) staining by using one representative cut surface of a frozen section of each SN. Intraoperative histologic examinations were optional and were performed on a case-by-case basis.

Surgical Procedure

After SN mapping, D2 or modified D2 gastrectomy was performed for all patients by using the therapeutic guidelines recommended by The Japan Gastric Cancer Association for standard care of this patient population.

Evaluation of SN Mapping for Gastric Cancer

The primary end point of the study was sensitivity to detect metastasis on the basis of SN status. Secondary end points included SN detection rate, number and distribution of identified SNs, and rate of adverse effects as a result of SN mapping. The pathologic status of SNs and all harvested non-SNs after D2 or modified D2 gastrectomy were examined by HE staining of one representative cut surface of a paraffin-embedded specimen.

Statistical Consideration

We reasoned that a sensitivity of 95% in patients with lymph node metastasis would indicate clinical usefulness, whereas a rate of 85% would be the lower limit of interest. On the basis of this assumption, we calculated that 89 patients were needed to provide a 90% power for a two-sided 0.05 level of a type I error. Taking ineligible patients into account, we planned to include 100 patients with lymph node metastasis. Assuming that approximately 20% of the patients in the study population had lymph node metastasis, the sample size was set at 500. Statistical analysis of the data was performed by using χ^2 and Fisher's exact tests.

RESULTS

Patients and Treatment

From July 2004 to March 2008, 433 patients were preoperatively enrolled onto this study. As shown in Figure 1, seven patients were

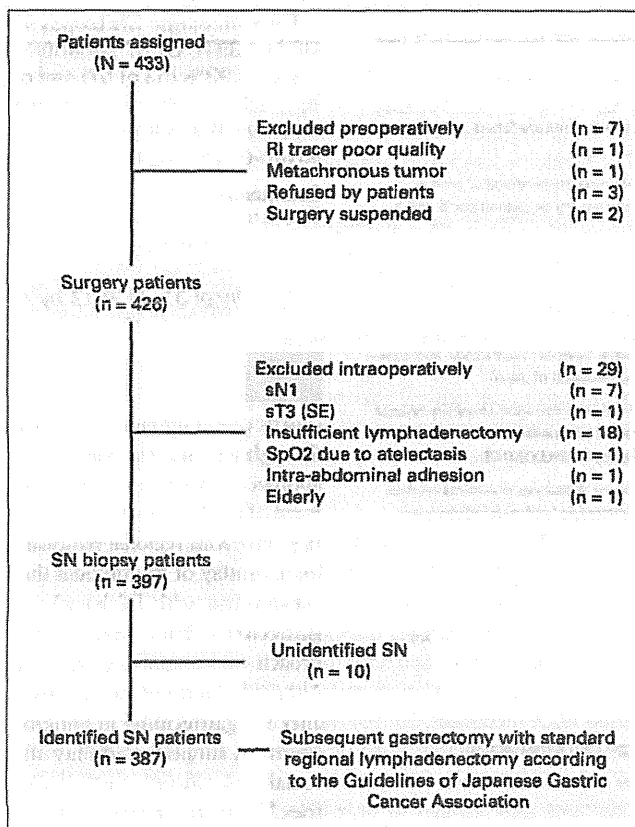


Fig 1. Flow of accrued patients. RI, radioisotope; SE, tumor penetration of serosa; SN, sentinel node; SpO₂, pulse oximeter oxygen saturation.

Table 1. Patient Characteristics (N = 397)

Characteristic	No.	%	G	A	L	P
Age, years						
Median	63					
Range	29-87					
Sex						
Male	264	66				
Female	133	34				
Location of tumor (in stomach)						
Upper third	76		5	6	41	24
Middle third	176		30	30	67	49
Lower third	145		31	22	63	29
cT factor						
T1	341	86				
T2	56	14				
Tumor size, cm (measured after gastrectomy)						
Median	3.0					
Range	0.6-10.0					

Abbreviations: A, anterior wall; G, greater curvature; L, lesser curvature; P, posterior wall.

preoperatively excluded and 29 others were excluded on the basis of intraoperative findings according to the protocol eligibility criteria. In 18 patients, the extent of lymphadenectomy was not sufficient for several reasons, including severe intra-abdominal adhesion, obesity, or the patients' and/or surgeon's desire for minimized gastrectomy, such as partial resection. Finally, 397 patients underwent SN biopsies (Table 1). We diagnosed 341 lesions (86%) as primary T1 lesions. In addition to the radioguided method, 363 patients (91%) underwent dye-guided SN mapping. Laparoscopy-assisted gastrectomy was performed in 161 patients (41%). Intraoperative histologic examinations were performed on frozen sections from 301 patients (76%).

Adverse Effects of SN Biopsy

No serious allergic reactions were observed after tracer injection, except for instances of transient pigmentation (0.3%) and decreased pulse oximeter oxygen saturation (0.8%), which might have been related to the intraoperative dye injection (Table 2). These reactions were observed intraoperatively and sufficiently controlled while the patient was under general anesthesia. As indicated in Table 2, there was no significant increase in the number of postoperative complications caused by the SN biopsy procedures or standard surgery.

Results of SN Biopsy

The SN detection rate determined by using the dual tracer method was 97.5% (387 of 397; Table 3). Three (30%) of the 10 patients with undetected SNs underwent radioguided mapping alone. Lymph node metastasis was diagnosed in 57 (14.7%) of 387 patients, and the incidence of lymph node metastasis was significantly higher in cT2 tumors than in cT1 tumors ($P < .001$). Of the 57 patients with lymph node metastasis, 53 (93.0%) showed positive SNs. The accuracy of metastatic status based on SN evaluation was 99.0% (383 of 387). In 32 (60.4%) of 53 patients with positive SNs, lymph node metastases were limited to only SNs. Of 21 SN-positive/non-SN-positive patients, 15 (71.4%) had metastatic non-SNs within SN basins and six (28.6%) had metastatic non-SNs located outside the SN

Table 2. Adverse Effects (N = 397)

Adverse Effect	No.	%
Administration of the tracers		
Allergic reaction to the radioactive tracer	0	0
Allergic reaction to the dye tracer	0	0
Intraoperative remarkable findings		
Pigmentation (transient)	1	0.3
SpO ₂ ↓ (transient)	3	0.8
Postoperative complications		
Pneumonia	2	0.5
Anastomotic leakage	1	0.3
Pancreatic leakage	2	0.5
Intra-abdominal abscess	5	1.3
Anastomotic stenosis	1	0.3
Small bowel obstruction	4	1.0
Bleeding	2	0.5
Thrombus/embolism	1	0.3

Abbreviation: SpO₂, pulse oximeter oxygen saturation.

basins but within the extent of the D2 lymph node dissection. Four patients had false-negative SN biopsy results of whom three had either pT2 or primary tumors > 4 cm or both (Fig 2A).

Diagnostic Accuracy of the Primary Tumor

We evaluated differences in clinical and pathologic tumor depth (UICC TNM Classification, 6th edition) and primary tumor diameter (Table 3). Notably, 314 (94.3%) of 333 cT1 (mucosa + submucosa) patients were diagnosed as pT1 (mucosa + submucosa), but only 26 (48.1%) of 54 cT2 (muscularis propria + subserosa) patients were diagnosed as pT2 (muscularis propria + subserosa). Regarding pT3 (tumor penetration of serosa), one (0.3%) cT1 and three (5.6%) cT2 patients (a total of four [1.0%] of 387 patients with cT1 or cT2) were diagnosed as pT3. Regarding tumor diameter, 78 (20.2%) of 387 tumors were > 4 cm.

Sensitivity of Intraoperative Pathologic Detection of Metastases in SNs Using Frozen Tissue Sections

Intraoperative examinations showed that nine patients were SN negative, but permanent tissue sections were SN positive. The sensitivity of metastatic SN detection that uses intraoperative frozen sections was 79% when based on patients and 70% when based on lymph nodes. In seven (78%) of these nine patients, metastatic spread was limited to the SNs. In the remaining two patients, metastases were limited to the area within the SN basins.

Distribution of SNs

The distribution of SNs is shown in Figures 2B to 2D. SNs were located outside the area of D2 lymph node dissection in 1% of patients with primary tumors in the upper third, 3% in the middle third, and 6% in the lower third of the stomach, respectively.

DISCUSSION

The results of this multicenter prospective trial demonstrated that SN mapping for gastric cancer with the dual tracer method is a feasible and safe procedure. The detection rate of SNs and the

Table 3. Results of SN Biopsy and Diagnostic Accuracy of Tumor Depth

Variable	All Patients (N = 397)		cT1 Patients (n = 341)		cT2 Patients (n = 56)		P
	No.	%	No.	%	No.	%	
SN identification							.64
Detected	387	97.5	333	97.7	54	96.4	
Undetected	10	2.5	8	2.3	2	3.6	
No. of identified SNs							.13
Mean		5.6		5.5		6.1	
± SD (per patient)		3.1		3.2		2.8	
pN factor	387		333		54		<.001
pN positive	57	14.7	32	9.6	25	46.3	
pN negative	330	85.3	301	90.4	29	53.7	
SN metastasis	57		32		25		.62
pSN positive	53	93.0	29	90.6	24	96.0	
pSN negative (false negative)	4	7.0	3	9.4	1	4.0	
SN/non-SN metastatic status	387		333		54		<.001
SN positive/non-SN negative	32	8.3	21	6.3	11	20.4	
SN positive/non-SN positive	21	5.4	8	2.4	13	24.1	
SN negative /non-SN negative	330	85.3	301	90.4	29	53.7	
SN negative/non-SN positive	4	1.0	3	0.9	1	1.9	
Pathologic T factor	387		333		54		<.001
T1 (M + SM)	339	87.6	314	94.3	25	46.3	
T2 (MP + SS)	44	11.4	18	5.4	26	48.1	
T3 (SE)	4	1.0	1	0.3	3	5.6	
T4 (SI)	0		0		0		

Abbreviations: M, mucosa; MP, muscularis propria; SD, standard deviation; SE, tumor penetration of serosa; SI, tumor invasion to adjacent structures; SM, submucosa; SN, sentinel node; SS, subserosa.

sensitivity of detection of regional lymph node metastasis by SN biopsy were comparable to previously reported data regarding breast cancer and melanoma.^{13,14}

Regarding indications for SN mapping, patients with clinically evident lymph node metastasis were excluded because the purpose of this technique was to identify clinically undetectable lymph node involvement. T3 or T4 tumors in which the anatomically natural lymphatic drainage routes might be obstructed or altered were also considered as not within the evaluation range of this study. Previous single-institution studies suggested that cT1 tumors would be the most suitable indication for this procedure. To confirm the proper indications of SN biopsy in terms of the depth of the primary lesions, patients with clinically T1 or T2 tumors with a primary lesion diameter of ≤ 4 cm were enrolled onto this prospective study. We concluded that SN mapping is indicated in cT1 lesions because the false-negative rate was significantly higher in cT2 tumors than in cT1 tumors in this study.

Our results also suggested that meticulous attention to an accurate preoperative diagnosis of the T factor is necessary to optimize SN mapping. Notably, the diagnostic accuracy of cT2 is not currently sufficient; therefore, the clinical application of SN mapping should be limited to cT1 tumors. Furthermore, if the primary tumor is diagnosed as cT1, but pT2 or deeper in patients who undergo function-preserving gastrectomy based on SN mapping, additional treatment, including surgery or chemoradiotherapy, should be considered.

The SN hypothesis is applied to patients at risk of lymph node metastasis, which is diagnosed by the characteristics of the primary tumor, but having clinically undetectable regional metastatic nodes, as confirmed by preoperative diagnostic imaging. Therefore, patients

indicated for endoscopic treatment such as endoscopic mucosal resection and endoscopic submucosal dissection were excluded from the selection criteria for SN biopsy (additional detail is provided in the Appendix, online only).^{15,16} Although an SN biopsy is technically feasible for lesions > 4 cm, the volume and injection points for the tracers must be considered in each case. Furthermore, tumors > 4 cm are not practical targets for minimally invasive and modified surgery based on SN status. We could not identify additional exclusion criteria such as the histologic type in this trial because of the limited number of patients with false-negative SN biopsy results. Furthermore, we found no clinical issues to account for the failure to identify SNs in the 10 patients with undetected SNs. Nonetheless, our results suggested that the dual tracer method might have been responsible for the higher SN detection rate compared with the radio-guided method alone.

At this time, radio-guided SN mapping combined with dye-guided real-time visualization of lymphatic vessels and SNs is recommended as a reliable SN detection method in gastric cancer. Although there remain several controversial points regarding performance of the actual procedure, such as the type of dye, the injection route (submucosal or subserosal), the volume of tracer, and the observation timing,¹⁷ the multicenter study group of the Japan Society of Sentinel Node Navigation Surgery has adopted an optimal procedure for SN mapping of gastric cancer from a previous single-institution experience. We chose to use technetium 99m tin colloid, which has a relatively large particle size. In our experience, tin colloid migrates into the SNs within 2 hours and remains there for > 20 hours until it is phagocytized by macrophages. Endoscopic injection enables us to accurately inject the tracer, even laparoscopically, compared with

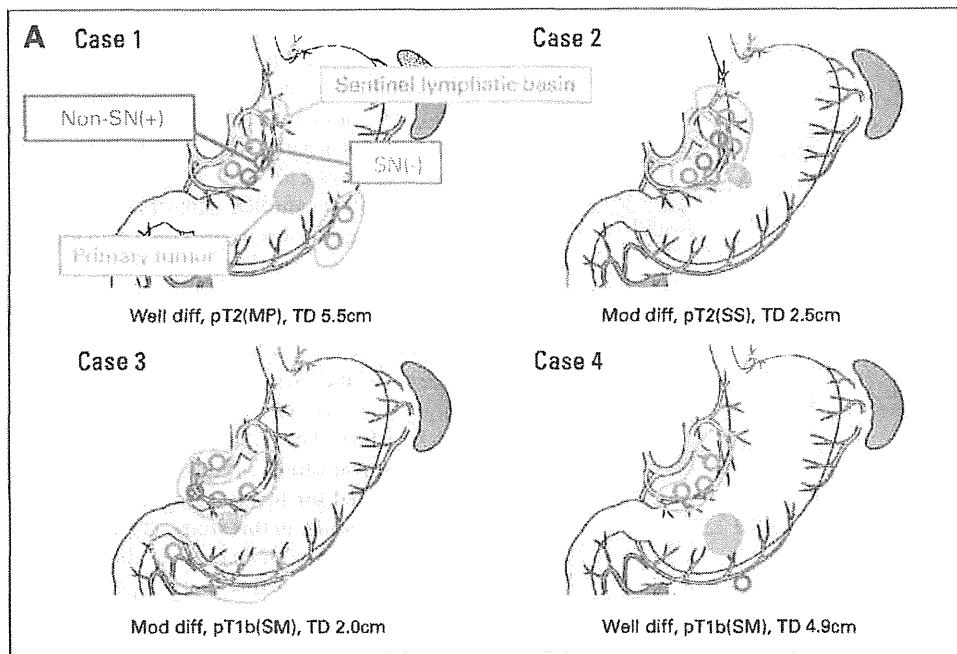


Fig 2. Distribution of identified sentinel nodes (SNs). (A) False-negative cases. Pink region, primary tumor; red circles, SNs (no metastasis); blue circles, nonsentinel nodes (metastatic); gold regions, sentinel node basins. Mod diff, moderately differentiated adenocarcinoma; MP, muscularis propria; SM, submucosa; SS, subserosa; TD, tumor diameter; Well diff, well differentiated adenocarcinoma. (B) Distribution and incidence of identified sentinel nodes: gastric cancer of the upper third of the stomach ($n = 75$). Blue circles, lymph nodes in the first compartment; red circles, lymph nodes in the second compartment; gold circles, lymph nodes in the third or other compartments. (C) Distribution and incidence of identified sentinel nodes: gastric cancer of the middle third of the stomach ($n = 175$). Blue circles, lymph nodes in the first compartment; red circles, lymph nodes in the second compartment; gold circles, lymph nodes in the third or other compartments. (D) Distribution and incidence of identified sentinel nodes: gastric cancer of the lower third of the stomach ($n = 137$). Blue circles, lymph nodes in the first compartment; red circles, lymph nodes in the second compartment; gold circles, lymph nodes in the third or other compartments. (B-D) The station number was described according to the Japanese Classification of Gastric Carcinoma¹²: (1) right cardiac lymph nodes, (2) left cardiac lymph nodes, (3), lymph nodes on lesser curvature, (4sa) lymph nodes along the short gastric vessels, (4sb) lymph nodes along the left gastroepiploic vessels, (4d) lymph nodes along the right gastroepiploic vessels, (5) suprapyloric lymph nodes, (6) intrapyloric lymph nodes, (7) lymph nodes along the root of left gastric artery, (8a) lymph nodes along the common hepatic artery, (9) lymph nodes along the celiac artery, (10) lymph nodes at the splenic hilum, (11p) lymph nodes along the proximal splenic artery, (11d) lymph nodes along the distal splenic artery, and (14v) lymph nodes along the superior mesenteric vein.

subserosal direct injection, although the latter might be easier during open surgery.

Intraoperative pathologic diagnosis was not mandatory in this study and was not available in 24% of the patients because of pathology policies in each institution. Intraoperative pathologic examinations are important for developing a future individualized function-preserving gastrectomy procedure on the basis of SN mapping. However, the main purpose of this multicenter trial was to verify the SN concept in gastric cancer surgery; therefore, we analyzed the histologic results of permanent tissue sections to assess the status of the SNs and other lymph nodes. Our results suggested that the sensitivity of intraoperative histologic diagnosis that uses an HE-stained section of one representative cut surface of a frozen section of a harvested SN is limited and may not be sufficient to provide reliable information for deciding the indications of limited lymph node dissection. Several reports described upstaging by more accurate and intensive examinations focused on SNs, which included step sections, immunohistochemical analysis, and molecular biologic techniques.¹⁸⁻²¹ Molecular assessment of SNs may be a variable tool to complement histologic examination for gastric cancers. Recently, we established a highly sensitive real-time reverse transcriptase polymerase chain reaction system to detect messenger RNA of cytokeratin 19, cytokeratin 20, and carcinoembryonic antigen in SNs of patients with gastric cancer.¹⁸ This system generated results within 80 minutes and might be avail-

able for intraoperative diagnosis in the future. Moreover, in all nine patients in this study with a false-negative intraoperative pathologic diagnosis, metastatic spread was limited to either the SNs or within the SN basins. We reasoned that SN basin dissection might be beneficial to future clinical applications of individualized minimally invasive gastrectomy based on intraoperative histologic diagnosis of SNs to amend the insufficiency of intraoperative pathologic diagnosis.

Generally, two types of SN sampling procedures for gastric cancer have been described. The pick-up method is a well-established and simple method that is currently used to assess breast cancer and melanoma. Miwa et al²² proposed the concept of SN basin dissection on the basis of their own data, in which SN basins contained true-positive nodes, even in patients with a false-negative SN biopsy. This concept was also valid in this prospective multicenter trial with only one exception. SN basin dissection is considered a minimally focused lymphadenectomy method for early gastric cancer with a reasonable safety net to avoid recurrence after a false-negative SN biopsy.

In 2004, the Japan Clinical Oncology Group (JCOG) conducted a multicenter prospective clinical trial of SN biopsy for cT1N0 gastric cancer.²³ The JCOG 0302 study was designed to evaluate the feasibility and accuracy of diagnosis using SN biopsy by the dye-guided method with intraoperative subserosal direct injection of indocyanine green. This study was designed as a simple and practical procedure to evaluate the applications of modified

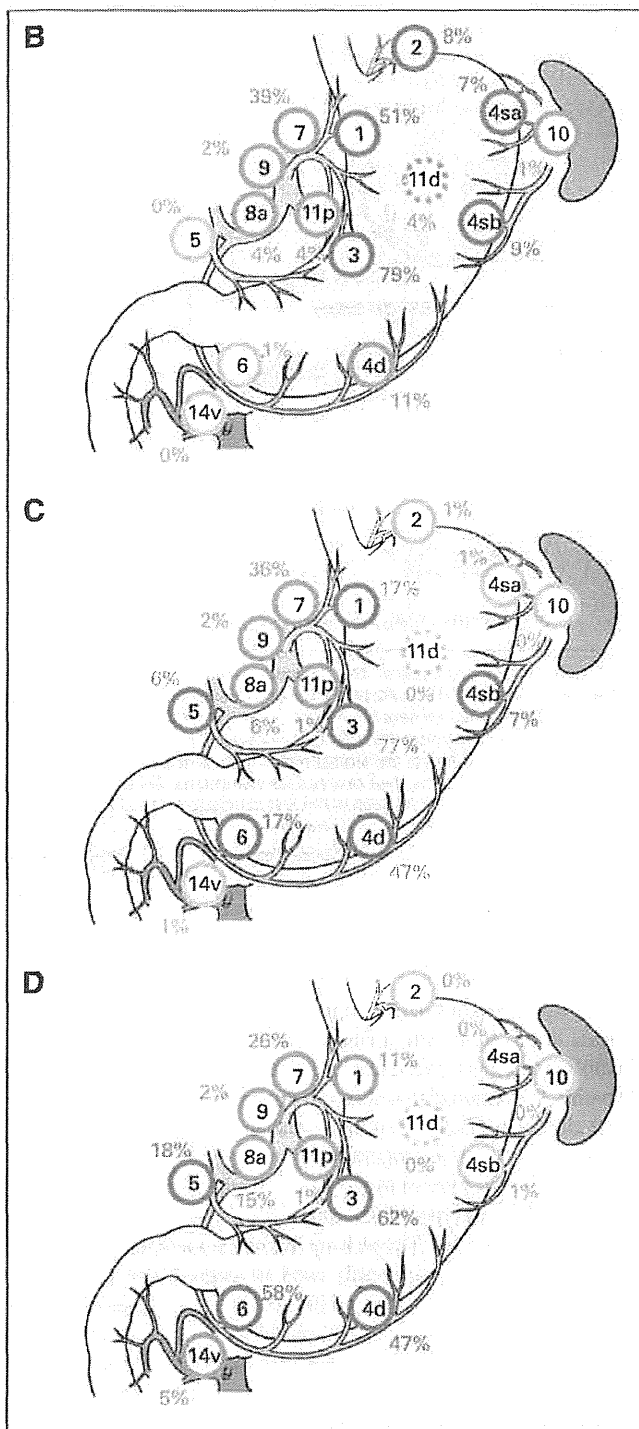


Fig 2. (Continued).

surgery without lymphadenectomy for SN-negative early gastric cancer. The details of the study have not yet been published since patient recruitment was terminated midway because of the unexpectedly high false-negative rate. Several factors were involved, including technical issues of the dye-guided method with direct injection of the tracer and limited sensitivity of intraoperative

histologic diagnosis of SN status. One of the most critical limitations in the JCOG 0302 study could be the fact that there were only five initial cases for training in each institution. In this multicenter study, 30 cases were required as the minimum initial learning phase to participate, which was based on a previous multicenter report regarding SN biopsies for breast cancer.²⁴

In future studies, appropriate indications for function-preserving gastrectomy, including proximal gastrectomy, segmental gastrectomy, pylorus-preserving gastrectomy, and partial resection for cT1N0 gastric cancer, should be individually determined on the basis of the SN mapping concept. Various types of laparoscopic function-preserving surgeries can be performed for patients with cancer who have negative SNs. Earlier recovery after surgery and preservation of quality of life in the late disease phases can be achieved by limited laparoscopic gastrectomy with SN navigation. Meanwhile, unexpected anatomic skip metastases might be accounted for by aberrant drainage routes from the primary lesion. As shown in this study, D2 gastrectomy was not always an effective method for harvesting the first draining nodes from a primary lesion. The distribution of sentinel lymphatic basins and SN status would be useful information for deciding on the extent of gastric resection.

On the basis of the findings in this prospective study, we designed our next randomized controlled trial to compare individualized gastrectomy based on intraoperative SN biopsy data with conventional distal/total gastrectomy (for further detail, see the Appendix). We believe that our next trial will demonstrate similar oncologic outcomes and superiority in postoperative quality of life for patients who have individualized gastrectomy, and it will further validate the clinical utility of SN mapping with SN basin dissection for early gastric cancer to achieve the goal of minimizing unnecessarily extensive surgery. Although there are several unresolved issues, SN navigation surgery presents a novel individualized, minimally invasive approach for early gastric cancer, both in terms of degree of incisional access and extent of function preservation.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) and/or an author's immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.
Employment or Leadership Position: None **Consultant or Advisory Role:** None **Stock Ownership:** None **Honoraria:** Yuko Kitagawa, Covidien Japan **Research Funding:** None **Expert Testimony:** None **Patents:** None **Other Remuneration:** None

AUTHOR CONTRIBUTIONS

Conception and design: Yuko Kitagawa, Shoji Natsugoe, Takashi Fujimura, Yoshikazu Uenosono, Shinichi Kinami, Junichi Sakamoto, Satoshi Morita, Takashi Aikou, Koichi Miwa, Masaki Kitajima

Collection and assembly of data: Yuko Kitagawa, Hiroya Takeuchi, Yu Takagi, Shoji Natsugoe, Masanori Terashima, Nozomu Murakami, Hironori Tsujimoto, Hideki Hayashi, Nobunari Yoshimizu, Akinori Takagane, Yasuhiko Mohri, Kazuhito Nabeshima, Yoshikazu Uenosono, Shinichi Kinami, Takashi Aikou, Koichi Miwa, Masaki Kitajima

Data analysis and interpretation: Yuko Kitagawa, Hiroya Takeuchi, Shoji Natsugoe, Yoshikazu Uenosono, Junichi Sakamoto, Satoshi Morita, Takashi Aikou, Koichi Miwa, Masaki Kitajima
Manuscript writing: All authors
Final approval of manuscript: All authors

REFERENCES

1. Shimada Y: JGCA (The Japan Gastric Cancer Association): Gastric cancer treatment guidelines. *Jpn J Clin Oncol* 34:58, 2004
2. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Gastric Cancer: Principles of Surgery, Version 2. 2011
3. Okines A, Verheij M, Allum W, et al: Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 21:v50-v54, 2010
4. Songun I, Putter H, Kranenbarg EM, et al: Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 11:439-449, 2010
5. Kitagawa Y, Fujii H, Mukai M, et al: The role of the sentinel lymph node in gastrointestinal cancer. *Surg Clin North Am* 80:1799-1809, 2000
6. Morton DL, Wen DR, Wong JH, et al: Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg* 127:392-399, 1992
7. Sirop S, Kanaan M, Korant A, et al: Detection and prognostic impact of micrometastasis in colorectal cancer. *J Surg Oncol* 103:534-553, 2011
8. Hiratsuka M, Miyashiro I, Ishikawa O, et al: Application of sentinel node biopsy to gastric cancer surgery. *Surgery* 129:335-340, 2001
9. Yano K, Nimura H, Mitsumori N, et al: The efficiency of micrometastasis by sentinel node navigation surgery using indocyanine green and infrared ray laparoscopy system for gastric cancer. *Gastric Cancer* 15:287-291, 2012
10. Uenosono Y, Natsugoe S, Ehi K, et al: Detection of sentinel nodes and micrometastases using radioisotope navigation and immunohistochemistry in patients with gastric cancer. *Br J Surg* 92:886-889, 2005
11. Lee JH, Ryu KW, Kim CG, et al: Sentinel node biopsy using dye and isotope double tracers in early gastric cancer. *Ann Surg Oncol* 13:1168-1174, 2006
12. Japanese Gastric Cancer Association: Japanese Classification of Gastric Cancer (ed 14). Tokyo, Japan, Kanehara Publishing, 2010
13. Wong SL, Balch CM, Hurley P, et al: Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Joint Clinical Practice Guideline. *J Clin Oncol* 30:2912-2918, 2012
14. Giuliano AE, Chung AP: Long-term follow-up confirms the oncologic safety of sentinel node biopsy without axillary dissection in node-negative breast cancer patients. *Ann Surg* 251:601-603, 2010
15. Sano T, Hollowood A: Early gastric cancer: Diagnosis and less invasive treatments. *Scand J Surg* 95:249-255, 2006
16. Gotoda T, Yanagisawa A, Sasako M, et al: Incidence of lymph node metastasis from early gastric cancer: Estimation with a large number of cases at two large centers. *Gastric Cancer* 3:219-225, 2000
17. Kitagawa Y, Kitano S, Kubota T, et al: Minimally invasive surgery for gastric cancer: Toward a confluence of two major streams—A review. *Gastric Cancer* 8:103-110, 2005
18. Shimizu Y, Takeuchi H, Sakakura Y, et al: Molecular detection of sentinel node micrometastases in patients with clinical NO gastric carcinoma with real-time multiplex reverse transcription-polymerase chain reaction assay. *Ann Surg Oncol* 19:469-477, 2012
19. Sagara Y, Ohi Y, Matsukata A, et al: Clinical application of the one-step nucleic acid amplification method to detect sentinel lymph node metastasis in breast cancer. *Breast Cancer* 20:181-186, 2013
20. Ballestar M, Dubernard G, Bats AS, et al: Comparison of diagnostic accuracy of frozen section with imprint cytology for intraoperative examination of sentinel lymph node in early-stage endometrial cancer: Results of Senti-Endo Study. *Ann Surg Oncol* 19:3515-3521, 2012
21. Ito T, Moroi Y, Oba J, et al: The prognostic value of a reverse transcriptase-PCR assay of sentinel lymph node biopsy for patients with cutaneous melanoma: A single-center analysis in Japan. *Melanoma Res* 22:38-44, 2012
22. Miwa K, Kinami S, Taniguchi K, et al: Mapping sentinel nodes in patients with early-stage gastric carcinoma. *Br J Surg* 90:178-182, 2003
23. Miyashiro I: What is the problem in clinical application of sentinel node concept to gastric cancer surgery? *J Gastric Cancer* 12:7-12, 2012
24. Cox CE, Salud CJ, Cantor A, et al: Learning curves for breast cancer sentinel lymph node mapping based on surgical volume analysis. *J Am Coll Surg* 193:593-600, 2001

Acknowledgment

We thank the following pathologists and radiologists for their contributions in this project: Makio Mukai and Tadaki Nakahara (Keio University School of Medicine), Suguru Yonezawa and Yoshiaki Nakabeppu (Kagoshima University Graduate School of Medical and Dental Sciences), Taizo Shiraishi and Kan Takeda (Mie University Graduate School of Medicine), Tamotsu Sugai and Shigeru Ehara (Iwate Medical University), Jun Matsubayashi and Mana Yoshimura (Tokyo Medical University), Hiroshi Kurumaya and Takeshi Kobayashi (Ishikawa Prefectural Central Hospital), Tohru Tanizawa and Hisao Ito (Graduate School of Medicine, Chiba University), Hideyuki Shimazaki and Shigeru Kosuda (National Defense Medical College), Kazuhiro Tasaki and Fumio Shishido (Fukushima Medical University), Yoh Zen and Norihisa Tonami (Kanazawa University), Naoya Nakamura (Tokai University), and Ken Shimizu and Yoshinori Satou (Saitama Social Insurance Hospital). We also thank Satomi Yana and Satoshi Kamiya for managing the database. We are indebted to J. Patrick Barron (Tokyo Medical University) for his review of this manuscript.

Appendix

Indication of Endoscopic Treatments

The indications of endoscopic treatments such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) were limited to the following: (1) mucosal tumors, (2) histologically differentiated-type adenocarcinomas, (3) tumors with diameters < 2 cm, and (4) no sign of ulceration of the lesion. If the primary tumor characteristics met these criteria, then lymph node metastasis was considered absent.¹⁵ Recently, Gotoda et al¹⁶ proposed an expansion of the ESD criteria to identify early gastric cancer without lymph node metastasis. According to the new criteria, a differentiated-type mucosal carcinoma of any size without ulceration or ulcer scarring and differentiated-type mucosal tumors < 3 cm with ulceration or ulcer scarring can be curatively resected endoscopically. Regarding the undifferentiated-type, the expanded criteria have been carefully revised to account for patients with a relatively high risk of lymph node metastasis. Sentinel node (SN) biopsy can be performed in patients with cT1N0M0 gastric cancer beyond these EMR/ESD criteria.

Our Next Trial

On the basis of the findings in this prospective study, we designed our next randomized controlled trial to compare individualized gastrectomy based on intraoperative SN biopsy data with conventional distal/total gastrectomy. In the next trial, the patients will be limited to those with cT1N0M0 gastric cancers, characterized by single lesions < 4 cm in size, who received no previous endoscopic treatment. In the individualized surgery group, according to the intraoperative pathologic examination results, minimized gastrectomy with SN basin dissection is indicated for patients with no SN metastases or standard gastrectomy with D2 lymph node dissection for patients with SN metastases. The 5-year recurrence-free survival rate will be the primary end point to compare the individualized gastrectomy group and the conventional distal/total gastrectomy group, and the 3-year recurrence-free survival, 3- to 5-year overall survival, diagnostic accuracy of SNs, and postoperative quality of life were chosen as secondary end points. SN basin dissection is considered a minimally focused lymphadenectomy method for early gastric cancer and a reasonable safety net to ameliorate an intraoperative pathologic misdiagnosis to avoid recurrence after a false-negative SN biopsy.

JOB SATISFACTION OF HEALTH-CARE WORKERS AT HEALTH CENTERS IN VIENTIANE CAPITAL AND BOLIKHAMSAI PROVINCE, LAO PDR

SENBOUNSOU KHAMLUB^{1,2}, MD. HARUN-OR-RASHID¹,
MOHAMMAD ABUL BASHAR SARKER¹, TOMOYA HIROSAWA¹,
PHATHAMAVONG OUTAVONG³ and JUNICHI SAKAMOTO¹

¹*Young Leaders' Program in Healthcare Administration, Nagoya University Graduate School of Medicine,
Nagoya, Japan*

²*National Tuberculosis Center, Hygiene and Prevention Department, Ministry of Health, Vientiane capital,
Lao PDR*

³*Monitoring and Evaluation Officer, Lao-Lux Development Programme, Vientiane Capital, Lao PDR*

ABSTRACT

The aim of this study was to assess job satisfaction levels among health-care workers and factors correlated with their overall job satisfaction. This cross-sectional study was conducted from July to September 2011 with 164 health-care workers using self-administered questionnaires on a six-point Likert scale. Categorical variables were reported using frequencies and median (interquartile range), while continuous data were using means and standard deviations. Spearman rho coefficients were computed to correlate the overall job satisfaction for each factor, Kruskal-Wallis and Mann-Whitney *U* tests were used to evaluate the differences between demographic characteristics on overall job satisfaction. Of the 164 respondents, the majority were females (65.85%). Other dominant variables were married (76.83%), age ≥ 41 years old (44.51%), certified health professional level (96.30%), nurse profession (59.10%), and working experience ≤ 5 years (55.49%). Participants were satisfied with 17 factors, but dissatisfied with salary levels at a mean score of (3.25). The highest satisfaction reported was for the freedom to choose the method of working with a mean score of 4.99, followed by the amount of variety on the job (4.96), amount of responsibility (4.90), and relationships with co-workers (4.90). The correlation coefficient between overall job satisfaction and main factors for job satisfaction-conflict resolution at work, relationships with co-workers, and organizational structure were (0.79), (0.76), and (0.71), respectively. There were statistically significant differences in age group, working experience and position ($P < 0.05$). In conclusion, health-care workers at health centers in Lao PDR were generally satisfied with their job except for their salary. The main factors that correlate with their overall job satisfaction were conflict resolutions at work, relationships with other co-workers, and organizational structure.

Key Words: Job satisfaction, Health-care workers, Laos

INTRODUCTION

Job satisfaction is defined by how employees feel about their jobs and different aspects of their

Received: April 26, 2013; accepted: July 11, 2013

Corresponding author: Mohammad Abul Bashar Sarker

Department of Healthcare Administration, Nagoya University Graduate School of Medicine,
65, Tsurumai-Cho, Nagoya 466-8550, Japan.

Phone/Fax: +81-52-744-2444, Email: basarcmc@yahoo.com

jobs.¹⁾ Job satisfaction is one of the important variables in work and organizational psychology, is regarded as an indicator of working-life quality,²⁾ and is a crucial variable used to determine the quality of health-care systems.

Health centers in the Lao People's Democratic Republic (Lao PDR) provide primary health-care for most of the people at the village level. Therefore, health center workers' job satisfaction is the most important indicator for determining their performance.

Many studies have shown that job satisfaction can be influenced by a wide variety of factors such as competitive pay, adequate staffing, a pleasant working environment, opportunities for personal and professional growth, a reasonable workload, supervision, recognition, noticeable progress of patients, positive relationships with co-workers, autonomy on the job, job security, career advancement and contingent rewards.³⁻⁵⁾ One study demonstrated the importance of job satisfaction to an organization in terms of its positive relationship with individual performance, employee relations, physical and mental health and satisfaction.⁶⁾ Thus, more satisfied employees tend to be more productive and creative.⁷⁾ The job satisfaction of health-care workers has a positive association with patients' satisfaction,^{8,9)} and contributes to the continuity of care.¹⁰⁾

Conversely, job dissatisfaction has a negative impact on the structure and work flows of organizations. Some negative impacts identified include greater non-conformance with procedures and policies, increases in work accidents, and organizational conflicts,¹¹⁾ that may increase the rate of medical errors, thus jeopardizing patient safety,¹²⁾ and higher employment costs,¹³⁾ that contribute to the shortages of health-care providers.¹⁴⁾ Job satisfaction is necessary to retain existing doctors, as well as to promote recruitment of new ones.¹⁵⁾ In short, the quality of health-care workers depends on the level of job satisfaction.²⁾

Several studies have demonstrated differences in how health-care providers feel about their jobs. Findings varied, with some research revealing job satisfaction,^{4,9,16-18)} while others disclosed dissatisfied health-care providers.^{3,15,19)} At the time of our study, there was no research that addressed job satisfaction among health-center workers in Lao PDR. Therefore, the aim of our study was to assess job satisfaction levels among health-care workers and the factors that correlated with their overall job satisfaction

MATERIALS AND METHODS

Design and participants

This cross-sectional study was conducted from July to September 2011 at the health centers in the Vientiane Capital and Bolikhamsai provinces based on convenient sampling. Health-care workers in our study included doctors, medical assistants, nurses, midwives, pharmacists, pharmacist assistants, laboratory technicians and hygienists. We included all staffs who worked at health centers in the two provinces. Health-care workers who were absent during the data collection period were excluded from the study.

Measures

Self-administered questionnaires were sent out. Among the total of 205 health-care workers from both provinces, 164 health-care workers (80% response rate) 101 in the Vientiane capital, and 104 in the Bolikhamsai responded to the questionnaire. Participants were informed beforehand regarding the conditions of participation and data handling.

Questionnaire

The questionnaires comprised two main parts; demography and job satisfaction. Demography

JOB SATISFACTION OF HEALTH-CARE WORKERS

included gender, marital status, age, professional level, profession, work experience, position, and work location. Job satisfaction partly consisted of 18 factors, such as satisfaction with physical working conditions, salary, promotional opportunities, relationships with co-workers, workload, support from supervisors, additional remuneration, responsibilities, working hours and others. For each factor, a respondent can choose from a six-point Likert scale representing various degrees of satisfaction: 1-very dissatisfied, 2-dissatisfied, 3-somewhat dissatisfied, 4-somewhat satisfied, 5-satisfied, and 6-very satisfied. Questions in this part were developed from a published study by Okaro in 2010.¹⁹⁾ The Cronbach's Alpha of the job satisfaction part was 0.89. That value indicates that the question was adequate as reliable.

Data analyses

We interpreted the level of job satisfaction using a mean score for each factor [19]. The overall levels of job satisfaction among health-care workers were classified as being dissatisfied if the sum of the scores for the different factors was between 18–54, while 55–72 was moderate and 73–108 was satisfied.²⁰⁾ Data from the questionnaires were analyzed using SPSS, version 19.0. Categorical variables were reported using frequencies and median (interquartile range), while continuous data (factors for job satisfaction) were using means and standard deviations. Spearman rho coefficients were then computed for correlating the overall job satisfaction levels and each factor. Kruskal–Wallis and Mann–Whitney *U* tests were used to evaluate the differences between selected demographic characteristics on overall job satisfaction. *P*-values less than 0.05 were considered statistically significant.

Ethics

This study was approved by the Ethical Committee of the Ministry of Health, Lao PDR. Informed consent was obtained by researchers from each participant.

RESULTS

Social demographic characteristics

The demographic data of 164 respondents are shown in Table 1. Participants in this study were mostly female (65.85%) and married (76.83%). The highest percentages were obtained from age groups ≥ 41 years of age (44.51%); whereas, the majority of females were from ≤ 30 years of age (43.50%). Most of the respondents had achieved a certified health professional level (96.30%). As for professions, most respondents were nurses (59.10%), followed by medical assistants (14.60%) and medical doctors (3.70%). Respondents with less than five years working experience accounted for (55.49%).

Job satisfaction for each factor

Table 2 shows the health-care workers rates of job satisfaction among various factors. They revealed that the health-care workers were satisfied with 17 factors and dissatisfied only with salaries, for a mean score of 3.25 (± 1.58). The highest level of satisfaction was reported for the freedom to choose one's method of working with a mean satisfaction score of 4.99 (± 0.87). This was followed by the level of job variety, the amount of responsibility, and their relationship with co-workers, giving mean scores of 4.96 (± 0.82), 4.90 (± 0.86) and 4.90 (± 0.80), respectively. Among males, the highest level of satisfaction was reported for the amount of variety on the job 5.14 (± 0.81), followed by freedom of working method 5.11 (± 0.82) and participation in decision making 4.98 (± 0.75). For females, it was the amount of responsibility 4.93 (± 0.82) and freedom

Table 1 Demographic characteristics of respondents (n=164)

Characteristics	Male N (%)	Female N (%)	Overall N (%)
Province			
Vientiane Capital	33 (58.9)	62 (57.4)	95 (57.93)
Bolikhamsai	23 (41.1)	46 (42.6)	69 (42.07)
Marital status			
Single	3 (5.4)	28 (25.9)	31 (18.90)
Married	52 (92.9)	74 (68.5)	126 (76.83)
Divorced/widowed	1 (1.8)	6 (5.6)	7 (4.27)
Age (Years)			
≤ 30	6 (10.7)	47 (43.5)	53 (32.32)
31 - 40	15 (26.8)	23 (21.3)	38 (23.17)
≥ 41	35 (62.5)	38 (35.2)	73 (44.51)
Professional level			
High diploma health profession	1 (1.8)	5 (4.6)	6 (3.70)
Diploma health profession	0 (0.0)	0 (0.0)	0 (0.00)
Certificated health profession	55 (98.2)	103 (95.4)	158 (96.30)
Profession			
Medical doctor	1 (1.8)	5 (4.6)	6 (3.70)
Medical assistant	11 (19.6)	13 (12.0)	24 (14.60)
Nurse	34 (60.7)	63 (58.3)	97 (59.10)
Midwife	3 (5.4)	6 (5.6)	9 (5.50)
Other (Pharmacist Assistant/ Laboratory Technician and Hygienist)	7 (12.5)	21 (19.4)	28 (17.10)
Working experience (Years)			
≤ 5	24 (42.9)	67 (62.0)	91 (55.49)
6 - 15	20 (35.7)	21 (19.4)	41 (25.00)
≥ 16	12 (21.4)	20 (18.5)	32 (19.51)
Position			
Chief/Vice Chief	32 (57.1)	57 (51.9)	88 (53.66)
Technical Staff	24 (42.9)	52 (48.1)	76 (46.34)
Health center located at home town			
Yes	38 (67.9)	79 (73.1)	117 (71.34)
No	18 (32.1)	29 (26.9)	47 (28.66)

of working method 4.93 (± 0.89), followed by the relationship with co-workers 4.92 (± 0.76) and amount of variety on the job 4.86 (± 0.81).

The overall job satisfaction of health-workers in health centers: 79.88% satisfied, 15.85% moderate, and 4.27% dissatisfied.

JOB SATISFACTION OF HEALTH-CARE WORKERS

Table 2 Job satisfaction for each factor on six-point Likert scale^a (n=164)

No.	Factors of job satisfaction	Male Mean (± SD)	Female Mean (± SD)	Overall Mean (± SD)
1.	Physical working place conditions	4.63 (1.00)	4.60 (0.93)	4.61 (0.96)
2.	Salary	3.41 (1.57)	3.17 (1.58)	3.25 (1.58)
3.	Opportunity to use abilities	4.71 (0.70)	4.69 (0.89)	4.70 (0.83)
4.	Opportunities for advancement	4.57 (1.09)	4.29 (1.29)	4.38 (1.24)
5.	Opportunity for training or education	4.41 (0.93)	4.61 (0.96)	4.54 (0.96)
6.	Additional remuneration for work	4.21 (1.56)	4.44 (1.34)	4.37 (1.43)
7.	Conflict resolution at work	4.91 (1.03)	4.74 (0.76)	4.80 (0.87)
8.	Support from supervisors	4.89 (0.70)	4.72 (0.90)	4.78 (0.84)
9.	Participation in decision making	4.98 (0.75)	4.69 (0.71)	4.79 (0.74)
10.	Utilization of skills	4.61 (0.84)	4.43 (0.99)	4.49 (0.95)
11.	Amount of variety on job	5.14 (0.81)	4.86 (0.81)	4.96 (0.82)
12.	Organizational structure	4.96 (0.93)	4.68 (0.74)	4.77 (0.82)
13.	Job security	4.68 (0.97)	4.40 (1.17)	4.49 (1.12)
14.	Freedom of working method	5.11 (0.82)	4.93 (0.89)	4.99 (0.87)
15.	Relationship with co-workers	4.86 (0.88)	4.92 (0.76)	4.90 (0.80)
16.	Amount of responsibility	4.84 (0.91)	4.93 (0.82)	4.90 (0.86)
17.	Total working hours	4.84 (0.78)	4.84 (0.86)	4.84 (0.36)
18.	General feeling about job itself	4.95 (0.90)	4.84 (0.84)	4.88 (0.86)

^aBased on scale of 1 to 6: 1=very dissatisfied, 2=dissatisfied, 3=somewhat dissatisfied, 4=somewhat satisfied, 5=satisfied and 6=very satisfied

Correlation between overall job satisfaction and each factor of satisfaction

In order to determine the main factors that were correlated with satisfaction and/or dissatisfaction with a job, the relationship between overall job satisfaction and job characteristics was analyzed (Table 3). Spearman's ratio demonstrated that the strongest correlation factor was in conflict resolution at work (0.79). Other factors that influenced satisfaction were relationships with co-workers (0.76) and organizational structure (0.71), respectively.

Comparison among demographic variables on overall job satisfaction

The Mann-Whitney U test revealed statistically significant differences among overall job satisfaction and age group, in which those age in between 31–40 years showed more job satisfaction than those with others ($P = 0.009$). As for working experience, respondents who worked >5 years were more satisfied with their job than those with ≤ 5 years of experience ($P = 0.017$). Those in leadership positions also showed more job satisfaction ($P < 0.001$). There were no differences in province, gender, marital status, professional level and profession as depicted in Table 4.

DISCUSSION

Our findings of this first study on job satisfaction in Lao PDR indicated that health-care

Table 3 Correlation between overall job satisfaction and each factor of satisfaction by Spearmen (n=164)

No.	job characteristics	Spearmen correlation coefficient	P-value ^a
1.	Conflict resolution at work	0.79	< 0.001
2.	Relationship with co-workers	0.76	< 0.001
3.	Organizational structure	0.71	< 0.001
4.	Amount of variety on job	0.68	< 0.001
5.	Participation in decision making	0.67	< 0.001
6.	Support from supervisors	0.66	< 0.001
7.	Job security	0.64	< 0.001
8.	Generally feeling about job itself	0.63	< 0.001
9.	Opportunities for advancement in profession	0.63	< 0.001
10.	Amount of responsibility	0.63	< 0.001
11.	Total working hours	0.62	< 0.001
12.	Opportunity to use your ability	0.62	< 0.001
13.	Salary	0.58	< 0.001
14.	Freedom to choose your method of working	0.56	< 0.001
15.	Physical working place conditions	0.53	< 0.001
16.	Utilization of skills	0.53	< 0.001
17.	Additional remuneration for work	0.47	< 0.001
18.	Opportunity for training or education	0.47	< 0.001

^aStatistical significance $P < 0.05$

workers in the two provinces were generally satisfied with their job, a finding similar to those in many previous studies.^{4, 9, 16-18)} We speculated that one possible reason for the overall high job satisfaction may be the location of this study, which was conducted in the capital and a nearby province that afforded a comfortable working environment, good infrastructure, and a convenient life. Therefore, workers in a big city were more interested in job satisfaction than those in a small city. Moreover, most respondents worked at health centers located in their own hometown (71.34%).

The three highest levels of satisfaction were the freedom to choose one's method of working, the level of variety in the job, and the amount of responsibility. That agrees with the findings of Cooper *et al.* who reported that health-care providers appreciated their freedom and independence to work, as well as enjoyed the responsibility and variety of their job.²¹⁾

Dissatisfaction with one's salary in our findings seems to be a common issue that is also evident in several other studies.^{2,5,14,15,17)} Many managers consider that the key motivation for their employees is pay, bonuses or raises. That suggests that health-care systems should provide a suitable salary and fringe benefits scheme to satisfy their workers and maintain their loyalty. In contrast, that does not seem to be a problem in Australia as evidenced by a previous study done in 2002. That discrepancy may be due to differences in the economic status of Australian health-care systems.²²⁾

The main factors that correlated with health-care workers' overall job satisfaction were conflict resolution at work, support from one's supervisor and relationship with co-workers. This is consistent with a study by Julian Montoro-Rodriguez, which indicated that job satisfaction

JOB SATISFACTION OF HEALTH-CARE WORKERS

Table 4 Comparison among demographic variables on overall job satisfaction by Kruskal–Wallis and Mann–Whitney U tests (n=164)

Variables	Number	Job satisfaction score		P-value ^a
		Median (IQR ^d)		
Province				
Vientiane Capital	95	86 (80–90)		0.839 ^b
Bolikhamsai	69	87 (71–90)		
Gender				
Male	56	87 (82–90)		0.192 ^b
Female	108	85 (74–90)		
Marital status				
Single	31	86 (79–89)		0.640 ^c
Married	126	86 (79–90)		
Divorced/Widow	7	84 (83–85)		
Age (Years)				
≤ 30	53	82 (70–88)		0.009 ^c
31–40	38	87 (80–92)		
≥ 41	73	86 (82–90)		
Professional level				
High diploma health profession/ Diploma health profession	6	78 (68–93)		0.880 ^b
Certificated health profession	158	86 (80–90)		
Profession				
Medical doctor	6	78 (68–93)		0.638 ^c
Medical assistance/Nurse/Midwife	130	86 (80–90)		
Pharmacist Assistant/Laboratory technician an Hygienist	28	85 (80–89)		
Working experience (Years)				
≤ 5	91	84 (72–89)		0.017 ^b
> 5	73	87 (83–91)		
Position				
Chief/Vice chief	88	88 (84–92)		< 0.001 ^b
Technical Staff	76	83 (71–88)		

^aStatistical significance $P < 0.05$; ^bP-value from Mann-Whitney U test; ^cP-value from Kruskal-Wallis test; ^dIQR, Interquartile Range.

was influenced by conflict resolution styles.²³⁾ The results of our study also suggest that by exhibiting transformational and contingent-reward leadership behaviors, there are strong relationships in health-care workers' job satisfaction with extrinsic and intrinsic motivators from their employers. Health-care leaders can utilize our results to identify how their leadership behaviors and interpersonal relationships with health-care workers may affect the work environment. Based

on our results, health-care workers' job satisfaction can be achieved by adopting participative leadership styles that encourage the workers to be involved in making decisions that have an influence on their work and their relationships with fellow workers. This finding was supported by Chen *et al.* who suggested that health-care leaders have the greatest opportunity to influence job satisfaction among health-care professionals.²⁴⁾ Rogatus *et al.* also showed that supervision and co-workers had a significant influence on job satisfaction.²⁵⁾

Demographic variables were used to locate the differences in overall job satisfaction. Our study found that health-care workers who put in longer hours and become seniors were more satisfied than their younger staffs. That may be because they adapted to their work and realized their work at the health center was important to people's health. That is consistent with previous research showing that professionals mature with age and accumulate more experience, which tends to foster a better adjustment to the work environment.²⁶⁾ High position was also found to result in higher job satisfaction. The probable reason is that the higher-position workers in public service will earn respectability from society. Similar previous studies have reported that holding a higher position tends to produce a high level of job satisfaction compared to those who lack such a high position.^{27,28)}

Our study has some limitations. First, it depends totally on convenience sampling, which emphasizes differences in demographic, geographical and socio economic characteristics of the provinces. So there is some difficulty in generalizing the results. In our analysis, however, we included the variables of provinces to estimate its effect, and our results showed no statistical difference in the satisfaction level of health workers from the two provinces. Second, our study covered only two provinces with relatively small sample sizes due to our limited resources. Thus, it may not be representative of all health-care workers of health centers in Lao PDR. However, all health-care workers in those provinces were approached, and their response rate was 80%, which was an acceptable level. However, a larger sample size and better sampling methods might result in a more conclusive comparison of job satisfaction in the future.

In conclusion, except for their salary, health-care workers at health centers in the Vientiane capital and Bolikhamsai Province, Lao PDR, were generally satisfied with their job. From our findings, we concluded that the main factors that correlated with their overall job satisfaction were conflict resolution at work, relationships with co-workers, and organizational structure.

ACKNOWLEDGEMENTS

The authors are grateful to Dr Xayphone NANTHAPHONE, Vientiane capital Tuberculosis Coordinator and other staffs who assisted us with data collection, and to all respondents who participated in this study. This work was supported in part, by a non-profit organization "Epidemiological & Clinical Research Information Network" (ECRIN).

REFERENCES

- 1) Mahmood A, Nudrat S, Asdaque MM, Nawaz A, Haider N. Job Satisfaction of Secondary School Teachers: A Comparative Analysis of Gender, Urban and Rural Schools. *Asian Social Science*, 2011; 7: 203–207.
- 2) Kinzl JF, Knotzer H, Traweger C, Lederer W, Heidegger T, Benzer A. Influence of working conditions on job satisfaction in anesthetists. *Br. J. Anaesth*, 2005; 94: 211–215.
- 3) Pillay R. Work satisfaction of professional nurses in South Africa: a comparative analysis of the public and private sectors. *BMC Human Resources for Health*, 2009; 7: 15.
- 4) Freeborn DK, Hooker RS. Satisfaction of physician assistants and other non-physician providers in a managed care setting. *Public Health Report*, 1995; 110: 714–719.

JOB SATISFACTION OF HEALTH-CARE WORKERS

- 5) Eker L, Tuzun EH, Dasakapan A, Surenkok O. Predictors of job satisfaction among physiotherapists in Turkey. *Journal of Occupational Health*, 2004; 46: 500–505.
- 6) Appleton K, House A, Dowell A. A survey of job satisfaction, sources of stress and psychological symptoms among general practitioners in Leeds. *BJGP*, 1998; 48: 1059–1063.
- 7) Mahmoud AL-Hussami, RN. A Study of Nurses' Job Satisfaction: The Relationship to Organizational Commitment, Perceived Organizational Support, Transactional Leadership, Transformational Leadership, and Level of Education. *European Journal of Scientific Research*, 2008; 22: 286–295.
- 8) Haas JS, Cook EF, Helen R, Puopolo SA, Burstinn HR, Cleary PD, Brennan TA. Is the professional satisfaction of general interests associated with patient satisfaction? *J Gen Intern Med*, 2000; 15: 122–128.
- 9) Buciuuniene I, Blazevičienė A, Bliudziute E. Health care reform and job satisfaction of primary health care physicians in Lithuania. *BMC Family Practice*, 2005; 6: 10.
- 10) Grembowski D, Ulrich CM, Paschane D, Diehr P, Katon W, Martin D, Patrick DL, Velice C. Managed Care and Primary Physician Satisfaction. *JABFP*, 2003; 16: 383–393.
- 11) Hoogendoorn WE, Bongers PM, Vet HCWD, Ariens GAM, Mechelen WV, Bouter LM. High physical work load and low job satisfaction increase the risk of sickness absence due to low back pain: results of a prospective cohort study. *Occup Environ Med*, 2002; 59: 323–328.
- 12) Fahrenkopf AM, Sectish TC, Barger LK, Sharek PJ, Lewin D, Chiang VW, Edwards S, Wiedermann BL, Landrigan CP. Rates of medication errors among depressed and burn tout residents: prospective cohort study. *BMJ*, 2008; 336: 488.
- 13) Freeborn DK. Satisfaction, commitment, and psychological well-being among HMO physicians. *West J Med*, 2001; 174: 13–18.
- 14) Goetz K, Campbell SM, Steinhäuser J, Broge B, Willms S, Szecsenyi J. Evaluation of job satisfaction of practice staff and general practitioners: an exploratory study. *BMC Family Practice*, 2011; 12: 137.
- 15) Kaur S, Sharma R, Talwar R, Verma A, Singh S. A study of job satisfaction and work environment perception among doctors in a tertiary hospital in Delhi. *Indian J Med Sci*, 2009; 63: 139–144.
- 16) Nylenna M, Gulbrandsen P, Forde R, Aasland OG. Unhappy doctor?. A Longitudinal study of life and job satisfaction among Norwegian doctor 1994-2002. *BMC Health Services Research*, 2005; 5: 44.
- 17) Burnard P, Morrison P, Phillips C. Job satisfaction among nurses in an interim secure forensic unit in Wales. *Aust N Z J Ment Health Nurs*, 1999; 8: 9–18.
- 18) Wada K, Arimatsu M, Higashi T, Yoshikawa T, Oda S, Taniguchi H, Kawashima M, Aizawa Y. Physician job satisfaction and working conditions in Japan. *J Occup Health*, 2009; 51: 261–266.
- 19) Okaro AO, Eze CU, Ohagwu CC. Survey of Job Satisfaction among Nigerian Radiographers in South-Eastern Nigeria. *European Journal of Scientific Research*, 2010; 39: 448–456.
- 20) Chen AH, Jaafar SN, Noor AR. Comparison of Job Satisfaction among Eight Health Care Professions in Private (Non-Government) Settings. *Malays J Med Sci. Forthcoming*, 2012.
- 21) Cooper CL, Rout U, Faragher B. Mental health, job satisfaction, and job stress among general Practitioners. *BJB*, 1989; 298: 366–370.
- 22) Ulmer B, Harris M. Australian GPs are satisfied with their job: even more so in rural areas. *Family Practice*, 2002; 19: 300–303.
- 23) Montoro-Rodriguez, J, Small, JA. The Role of Conflict Resolution Styles on Nursing Staff Morale, Burnout, and Job Satisfaction in Long-Term Care [abstract]. *J Aging Health*, 2006; 18: 385–406.
- 24) Chen HC, Beck LS, Amos LK. Leadership styles and nursing faculty job satisfaction in Taiwan. *Journal of Nursing Scholarship*, 2005; 37: 374–380.
- 25) Rogatus L. Mpeka. A study to examine the determinants of job satisfaction for professional accountants in Tanzania [abstract]. *AAJA*, 2012; 3: 15–33.
- 26) Shah MA, Al-Enezi N, Chowdhury RI, Otabi MA. Determinants of job satisfaction among nurse in Kuwait. *AJAN*, 2004; 21: 10–16.
- 27) Abdullah MM, Uli J, Parasuraman B. Job satisfaction among secondary school teachers. *Jurnal Kemanusiaan*, 2009; 13: 11–18.
- 28) Nielsen I, Smyth R. Job satisfaction and response to incentives among China's urban workforce. *The Journal of Socio-Economics*, 2008; 37: 1921–1936.

**KNOWLEDGE, ATTITUDES AND BARRIERS OF
PHYSICIANS, POLICY MAKERS/REGULATORS
REGARDING USE OF OPIOIDS FOR CANCER PAIN
MANAGEMENT IN THAILAND**

PORNSUREE SRISAWANG^{1,2}, MD. HARUN-OR-RASHID¹, TOMOYA HIROSAWA¹
and JUNICHI SAKAMOTO¹

¹*Young Leaders' Program in Healthcare Administration,
Nagoya University Graduate School of Medicine, Nagoya, Japan*
²*Narcotics Control Division, Food and Drug Administration, Nonthaburi, Thailand*

ABSTRACT

The efficacy of opioids for cancer pain has been proven and the World Health Organization (WHO) three-step ladder has been recommended for cancer pain relief. However, undertreatment of cancer pain has still been reported in Thailand. Identification of barriers to opioid use by the physicians and policy makers/regulators, and their level of knowledge and attitudes concerning its use are influential factors for cancer pain management (CPM). This study was performed to assess the knowledge and attitudes physicians and policy makers/regulators have regarding use of opioids for CPM. Barriers to opioid availability were also studied. A self-administered questionnaire was mailed to 300 physicians and distributed to 58 policy makers/regulators from September to October 2011. A total of 219 physicians and 47 policy makers/regulators completed the questionnaire. Of the physicians 62.1% had inadequate knowledge and 33.8% had negative attitudes. Physicians who did not know the WHO three-step ladder were more likely to have less knowledge than those having used the WHO three-step ladder (OR = 13.0, $p < 0.001$). Policy makers/regulators also had inadequate knowledge (74.5%) and negative attitudes (66.0%). Policy makers/regulators who never had CPM training were likely to have more negative attitudes than those having had training within less than one year (OR = 35.0, $p = 0.005$). Lack of training opportunities and periodic shortages of opioids were the greatest barriers to opioid availability for physicians and policy makers/regulators, respectively. The strengthening of ongoing educational programs regarding opioid use for CPM, and cooperation among key groups are needed.

Key Words: Policy makers, Regulators, Opioids, Cancer pain management, Thailand

INTRODUCTION

Cancer is one of the leading causes of death worldwide.¹⁾ In Thailand, the death rate per 100,000 people from cancer has increased more than two-fold in the past two decades, from 36.8 in 1989 to 87.4 in 2009.²⁾ Pain is a very common symptom in cancer patients, and has a great influence on their overall quality of life.³⁾ Therefore, adequate relief of pain is recognized as a patient's right.⁴⁾ In 1986, the World Health Organization (WHO) developed a set of guidelines

Received: January 23, 2013; accepted: June 3, 2013

Corresponding author: Pomsuree Srisawang, MS, MPH, BSc in Pharm

Narcotics Control Division, Food and Drug Administration, Nonthaburi 11000, Thailand

Phone: +66-2590-7794, Fax: +66-2590-7706, E-mail: iamyama2009@hotmail.com

for cancer pain management (CPM) based on the three-step ladder, which indicated opioids as the drug of choice for the treatment of moderate to severe pain.⁵⁾ Despite the clear WHO recommendations, there are still numerous studies reporting inadequately managed cancer pain in many countries including Thailand.^{6,7)}

Besides the pain management index, the increase of morphine consumption is another indicator of national progress toward improving cancer pain relief, as it is the drug of choice for the management of severe cancer pain and is on the WHO essential drug list.⁸⁾ Therefore, increased opioid consumption can be expected to reflect improved quality of pain control. Despite increases in the annual per capita morphine consumption from 0.29 mg in 1999 to 1.16 mg in 2010, Thailand's morphine consumption continues to be significantly lower than the global mean and remains lower than in many Asian countries.^{9,10)} As a result, there are still many cancer patients suffering from unrelieved pain in Thailand.

Barriers against adequate pain management are as follows: 1) patient-related barriers¹¹⁾ ; 2) professional-related barriers¹²⁻¹⁵⁾ ; and 3) system-related barriers.¹⁶⁾ This study evaluated barriers to opioid use set by policy makers/regulators and physicians, in addition to their knowledge and attitudes, because we consider that policy makers/regulators are important components involved in CPM using opioids. Their policies have the potential to either promote or interfere with CPM.¹⁷⁾ If policy makers and regulators have misconceptions and negative attitudes about opioids for CPM, they can create barriers to the adequate availability and access to them.

The Narcotics Control Division, Food and Drug Administration, Thailand (Thai FDA), has the responsibility of supplying category II opioid narcotics, such as morphine, for medical use in hospitals throughout the country. The regulators in this division have the responsibility of regulating narcotics specified in the Narcotics Act B .E. 2522 (1979). The Narcotics Control Committee plays the key role as policy maker by taking charge of submitted opinions and giving approval regulations for the Minister of Public Health regarding the Narcotics Act.¹⁸⁾

A recent study in Thailand showed that the majority of participating interns who recently graduated from the faculty of medicine demonstrated positive attitudes toward opioid usage for CPM. However, a significant number of them had incorrect knowledge regarding it.¹⁹⁾ Another study of physicians and nurses in a hospital revealed their insufficient knowledge about the optimal use of opioids, and inappropriate pain assessment including negative attitudes towards addiction and tolerance.²⁰⁾ These previous studies had limitations related to generalizability, and they lacked consistency. Furthermore, there has been no published study among Thai policy makers and regulators in this regard. Therefore, it was necessary to conduct this study with the objective of assessing the knowledge and attitudes of physicians, policy makers and regulators regarding opioids for CPM in Thailand. The associations of their knowledge and attitudes with background characteristics were evaluated. Their perceptions regarding the barriers to opioid availability were also studied because it is necessary to improve the availability of opioids in any country.²¹⁾

MATERIALS AND METHODS

This cross-sectional study was conducted in Thailand among two groups of participants from September to October 2011. The first group was physicians working in the hospitals which purchased category II opioids from the Thai FDA. The questionnaire with a cover letter from the Thai FDA was mailed to a simple random sample of 300 hospitals, and then the director of each hospital assigned one physician involved in treating cancer to complete the questionnaire. If no reply was received after one month, a phone call was made to the hospital requesting them

OPIOIDS FOR CANCER PAIN IN THAILAND

to send the completed questionnaire. For the second group, policy makers and regulators were consolidated into one category which consisted of 19 policy makers of the Narcotics Control Committee and 39 regulators of the Narcotics Control Division, Thai FDA. The questionnaires were administered to 19 policy makers on a meeting day and to 39 pharmacists who had been working as regulators for at least one year.

The self-administered questionnaire was adapted from previous studies with a modification to suit Thailand's situation, and was translated into Thai.^{14,15,19-24} The questionnaire was composed of four parts. The first part included background characteristics. The second and third parts covered knowledge (11 items with 7 negative and 4 positive) and attitudes (8 items with 6 negative and 2 positive) regarding opioids usage, the Narcotics Act, and the availability of opioids for CPM, respectively. Knowledge and attitudes items were arranged in a five-point Likert scale with options of "strongly disagree," "disagree," "uncertain," "agree" and "strongly agree." For the positive questions, the responses of "strongly agree" or "agree" were the correct answers for knowledge, and the desirable answers for attitudes. For the negative questions, "strongly disagree" or "disagree" were the correct answers for knowledge and the desirable answers for attitudes. The final part of the questionnaire covered perception regarding barriers to opioid availability for CPM (12 items). The participants were asked to identify each item concerning barriers with "not a problem," "minor problem," "don't know," "moderate problem" or "serious problem." The responses of "serious problem" were taken for analysis. Content validity was determined by a panel of three experts having expertise in opioid use for CPM. Reliability was assessed by using Cronbach's alpha. The values were 0.78 for knowledge items, 0.63 for attitude items and 0.86 for barrier items.

Descriptive statistics were computed for all items. We scored knowledge items and attitudes items as "1" for each correct or desirable answer, and "0" for each incorrect or non-desirable answer. The total knowledge score and total attitude score were computed for each participant. Inadequate knowledge and negative attitudes were defined as correctly answering less than 70% of the knowledge items (scoring less than 8 out of 11 points), and by answering less than 70% of attitude items (scoring less than 6 out of 8 points), respectively. We applied a 70% cut-off point from a previous study in the Philippines.²⁴ Logistic regression was used to identify associations of background characteristics with inadequate knowledge and negative attitudes. The chi-square test was performed to compare the serious perception of barriers among the two groups of participants. The Statistical Package for Social Science (SPSS) program version 19.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses. A *P* value of < 0.05 was considered statistically significant.

This study was approved by the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health of Thailand in September 2011. Anonymity and confidentiality were maintained throughout.

RESULTS

Background characteristics

We received responses to the questionnaires from 219 (73%) of the 300 physicians and 47 (81%) of the 58 policy makers/regulators. The overall response rate was 74%. Table 1 presents the background characteristics of participants. Physicians and policymakers/regulators were similarly distributed over the categories regarding the last time they received CPM education or training, with no significant difference. Additionally, 42.5% of physicians and 51.1% of policy makers/regulators reported that they had never had CPM education or training. Fifty-eight percent of

Table 1 Background characteristics of participants

Characteristics	Physicians (n=219)		Policy makers/ Regulators (n=47)		P value ^a
	N	(%)	N	(%)	
Gender					0.033
Male	126	(57.5)	19	(40.4)	
Female	93	(42.5)	28	(59.6)	
Age (y)					0.010
≤ 35	110	(50.2)	15	(31.9)	
36–45	64	(29.2)	13	(27.7)	
≥ 46	45	(20.5)	19	(40.4)	
Last time in cancer pain management education or training (y)					0.588
< 1	30	(13.7)	6	(12.8)	
1–5	69	(31.5)	14	(29.8)	
> 5	27	(12.3)	3	(6.4)	
Never	93	(42.5)	24	(51.1)	
Medical specialty					
Board certificate					
Anesthesiology	28	(12.8)			
Surgery	26	(11.9)			
Oncology	13	(5.9)			
Internal medicine	25	(11.4)			
Family medicine	13	(5.9)			
Pediatrics	6	(2.7)			
Obstetrics and Gynecology	8	(3.7)			
Others	8	(3.7)			
General Practice	92	(42.0)			
Hospital type					
Community hospital	130	(59.4)			
General hospital	24	(11.0)			
Regional hospital	22	(10.0)			
Cancer center	6	(2.7)			
Medical school hospital	7	(3.2)			
Private hospital	25	(11.4)			
Others	5	(2.3)			
Number of cancer patients being cared for in the past 6 months					
≤ 10	117	(53.4)			
11–30	64	(29.2)			
≥ 31	38	(17.4)			
Use of the WHO ^b three-step ladder					
Yes	110	(50.2)			
No	44	(20.1)			
Don't know the WHO ^b three-step ladder	65	(29.7)			
Be a member of the palliative care team					
Yes	79	(36.1)			
No	140	(63.9)			

^a P value by Chi-square test; ^b WHO: World Health Organization