the results of the first year's survey were published in the *Tohoku Journal of Experimental Medicine*[2] in English (the first such report from Japan ever to be published). Next, a report on the 3-year survey from 1951 to 1953 was published in the *Journal of the National Cancer Institute*,[3] in 1957. Segi adopted a new system that was used in the United States population for reporting and analyzing cancer incidence (so-called age-adjusted incidence) in Japan, and compared the cancer incidences between the two populations. Later, he and colleagues used the world population in 1950 as a base population for an international comparison of incidence and mortality rates.[4] After an actual 3-year survey, the first population-based cancer registry for epidemiological purposes was established to collect data on cancer patients. The new registry was set up in 1959 within the Department of Public Health at the Tohoku University School of Medicine, with the support of a grant from the National Cancer Institute of the United States.[5,6]

In 1957 and 1958, respectively, the cities of Hiroshima and Nagasaki established population-based cancer registries, in cooperation with local medical associations, to follow-up survivors of the atomic bombings of the two cities. These special-purpose registries have been operated by the Atomic Bomb Casualty Commission (ABCC)–Radiation Effects Research Foundation (RERF) to investigate the long-term effects of atomic bomb radiation on human health.[7]

In 1962, the prefectural governments of Aichi and Osaka, in cooperation with prefectural medical associations, established population-based cancer registries.[8] In ensuing years, this type of population-based cancer registry spread to Kanagawa (1970), Tottori (1971), Kochi (1973), and Chiba (1975) prefectures. Around the time when the Law on Health and Medical Services for the Aged was enacted, in 1983, population-based cancer registries were operating in 14 prefectures throughout Japan and in two cities. The new law recommended that all prefectural governors establish cancer registries as a support for the planning of cancer control programs and the assessment of cancer screenings. Registries were established in 19 prefectures promptly after the law was enacted. As of 2007, there were population-based registries in 35 of Japan's 47 prefectures and one city (see column headed "Prefecture/city" in Table 1).

Japan's contribution to the establishment of the International Association of Cancer Registries (IACR)

At the sixth International Congress of the International Union against Cancer (UICC), held in Tokyo in October 1966, Dr. Segi and Dr. Takamune Soda invited 47 people from 26 countries to take part in a satellite meeting on cancer registries, including 17 physicians then involved in the registries in Japan. During the meeting, Drs. William Haenszel and Sidney J. Cutler proposed the foundation of an international association for the exchange of information and the promotion of cancer registries worldwide. Not everyone agreed with the proposal or was convinced of the need for such an association. After clearing many roadblocks and difficulties entailed in the forming of an international association, a subcommittee, set up by Segi and others, concluded that an international association would encourage the development of cancer registries. The objective of the association would not be to compete with or oppose the World Health Organization (WHO), the International Agency for Research on Cancer (IARC), or the UICC, but to support their activities. Shortly afterwards, the International Association of Cancer Registries (IACR) was established. The physicians involved credited the establishment of the association in large measure to the foresight and industry of Dr. Segi.[9]

The first annual meeting of the IACR was held in 1970 in Houston, USA, chaired by Dr. Cutler. The sixth annual meeting was held in 1984 in Fukuoka, Japan, chaired by Dr. Takao Shigematsu.

History of national cancer control programs in Japan

Japan's first nationwide cancer control surveillances were the three National Cancer Surveys conducted by the Ministry of Health and Welfare in 1958, 1960, and 1962. These were followed by the first national cancer program, in 1966. The surveys and program shared five common goals: to promote cancer education, to promote cancer screening, to establish cancer-oriented medical facilities, to train health-care providers specialized in cancer treatment, and to promote cancer research. Regrettably, the cancer registration system was not included among these goals. Fourth and fifth National Cancer Surveys were conducted in 1979 and 1989, respectively, but no cancer registry system materialized.

The Japanese government implemented a Comprehensive 10-Year Strategy for Cancer Control (1984–1993) and a New 10-Year Strategy to Overcome Cancer (1994–2003) as nationwide programs to contend with cancer. In 2004, it launched the Third-Term 10-Year Comprehensive Strategy for Cancer Control to promote cancer research and disseminate high-quality cancer medical services. The chief aim was to "drastically reduce cancer morbidity and mortality." This latest strategy includes measures not only to promote cancer research but also measures to prevent cancer, improve the quality of cancer care, promote social support systems, and establish more effective systems for monitoring cancer incidence and survival (see Table 1, column headed "National cancer programs").

Activities of the Research Group for Population-Based Cancer Registration and the establishment of the Japanese Association of Cancer Registries (JACR)

In 1975, Dr. Isaburo Fujimoto organized the Research Group for Population-Based Cancer Registration (hereafter, the Group) in Japan with funds from a grant-in-aid under the National Cancer Research Promotion Program.

Table 1. History of cancer control programs in Japan in terms of cancer registration

Years cancer registration started	Prefecture/city	Research Group activities	National cancer programs	Laws, guidelines, conferences
1950s	Miyagi (1951–1953 survey) Hiroshima City (1957) Nagasaki City (1958) Miyagi (1959)		• The First National Cancer Survey (1958)	
1960s	Aichi, Osaka, Hyogo	• Subsidy for cancer research by Ministry of Health and Welfare started	• The Second National Cancer Survey (1960) • The Third National Cancer Survey (1962) • First cancer program implemented (1966)	• International Association of Cancer Registries (IACR) founded (1966)
1970s	Yamagata, Chiba, Kanagawa, Kochi, Tottori, Hokkaido	• Research Group for Population-Based Cancer Registration established (1975–1980; chairperson, Dr. Fujimoto)	• The Fourth National Cancer Survey (1979)	• First annual meeting of IACR, Houston, United States (1970)
1980s	Fukui, Nagasaki Prefecture, Saga, Yamaguchi, Shiga, Toyama, Okinawa, Kyoto, Aomori, Nara	• Research Group for Population-Based Cancer Registration established (1981–1986; chairperson Dr. Fukuma) • Research Group for Population-Based Cancer Registration established (1987–1992; chairperson Dr. Fujimoto)	• Comprehensive 10-Year Strategy for Cancer Control (1984–1993) • The Fifth National Cancer Survey (1989)	• Law on Health and Medical Services for the Aged (1983) • Sixth annual meeting of IACR, Fukuoka, Japan (1984)
1990s	Akita, Okayama, Niigata, Kumamoto, Iwate, Tochigi, Ibaragi, Ishikawa, Gunma, Gifu, Tokushima, Ehime, Kagoshima, Kagawa	• Japanese Association of Cancer Registries (JACR) founded (1992) • Research Group for Population-Based Cancer Registration established. (1993–1995, chairperson, Dr. Hanai) • Research Group for Population-Based Cancer Registration established (1996–2001, chairperson Dr. Oshima)	• New 10-Year Strategy to Overcome Cancer (1994–2003)	• Guidelines for confidentiality in the cancer registration scheme (1996)
2000s	Hiroshima Pref. Yamanashi	• Research Group for Population-Based Cancer Registration established (2002–2007, chairperson Dr. Tsukuma) • The Japan Cancer Surveillance Research Group (2004–2013, chairperson Dr. Sobue)	• Third-Term Comprehensive 10-Year Strategy for Cancer Control (2004–2013) • Action Plan 2005 for Promoting Cancer Control (2005)	• Ethics guidelines for epidemiological studies (2002) • Health Promotion Law (2003) • Private Information Protection Law (2004) • Guidelines for the appropriate handling of personal information by medical and care-related enterprises (2004) • Guidelines on confidentiality in cancer registries (revised, 2005) • Cancer Control Act implemented (2007)

The meetings of this Group are held annually. This research group has been continuing its work until now, under the direction of five successive chairpersons – Fujimoto himself, followed by Drs. Seigo Fukuma, Aya Hanai, Akira Oshima, and Hideaki Tsukuma. Here we cite five achievements of the Group to promote the standardization of registration procedures.

- First, the Group has been responsible for two major publications (the *Guidelines for population-based cancer registration in Japan*,[10] published in 1975 and the *Standardized methods of population-based cancer registries*,[11] published in 1977) and has translated a third into Japanese (*Cancer registration: principles and methods*, edited by Jensen et al. (translated in 1978). The *Guidelines* *for population-based cancer registration in Japan* have been revised three times, in 1977, 1986, and 1999.[12]

- Second, the Group has widened the scope and coverage of the various registries open in Japan, bringing them closer to completion.
- Third, the Group has prepared annual cancer statistics on items such as cancer incidence and survival rates by cancer type, with data from all of the member registries.
- Fourth, the Group has published the *Guidelines for confidentiality in the cancer registration scheme* [13] (in 1996).
- Fifth, twice a year, the Group has provided training course schedules and lectures for tumor registrars at the National Cancer Center. It also produces Japanese translations of the SEER program self-instruction manuals for tumor registrars, with permission from the Surveillance, Epidemiology, and End Results (SEER) program.
- Sixth, the Group has promoted the use of registry data for epidemiological research and for the planning and evaluation of the cancer control programs of the national government and municipal governments in Japan.

Population-based cancer registries have been introduced in many prefectures, beginning before the enactment of the Law on Health and Medical Services for the Aged in 1983. Information in these registries is provided on a voluntary basis by doctors and medical institutions, under the jurisdiction of the prefectures. However, the data collected and the systems used to manage the data differ from prefecture to prefecture. The Japanese Association of Cancer Registries (JACR) was organized in 1992 to promote standardization of the registry process and to improve the quality of registry data. The JACR holds annual scientific and procedural meetings to exchange information and provide training for newcomer registrars. Association members introduce their registries and staff on the JACR website (http://www.cancerinfo.jp/jacr/). The association sends its members a JACR monograph once a year and a newsletter every 6 months (see column headed "Research Group activities" in Table 1)

Changes in registry items and data management systems

Figure 1 shows a typical population-based cancer registry system in Japan. The doctors at hospitals and clinics send cancer reports to the medical association of their prefecture. The medical association, in turn, bundles the reports and sends them to a cancer registry central office each month. Another department in the prefectural government, meanwhile, sends copies of all of the death certificates issued over the past month in the prefecture to the same central office. Personnel in the central office collate all of the cancer reports and death certificates, eliminating duplicate registrations.

In the first cancer survey carried out by Segi,[2] the following information was collected for each patient: name, address, sex, age, date of first symptom, diagnosis, cancer site, and the method used to confirm the cancer diagnosis (microscopic, surgical, by X-ray, other). Once collected, the data were managed by hand using a card system or a hole-sort card system. In the 1960s, a selector machine system using standard cards with 80 columns was introduced. Each piece of information on a cancer case was coded as a number (from 0 to 9) and punched or marked at one point in one column (or at two points in one column to represent alphanumeric characters in English). As only 80 columns were available per card, the data to be registered in the cancer registries had to be selected very carefully.

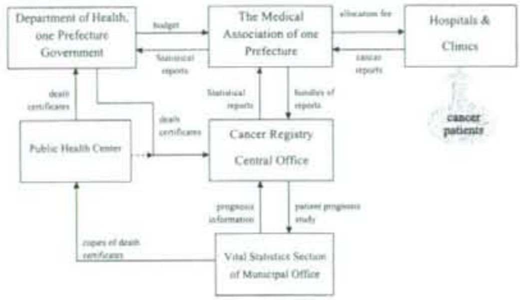

Fig. 1. Typical system of a population-based cancer registry in Japan

In the 1970s, some municipal governments and hospitals began using general computers. The registries at Hiroshima, Nagasaki, and Osaka were computerized forthwith. The conventional media for storing data in those days were paper tape, 80-column cards, open-reel tapes, and 8-inch floppy disks. As time-sharing systems (TSS) had yet to be adopted, all operations of the cancer registry were performed by batch processing. Then, in about 1980, the Osaka Population-Based Cancer Registry developed a semicomputerized collation method for linking records together using a general computer. This new method has been helpful not only for the routine task of registration but also for linking with files on other populations outside the registry.[14-16]

Now that we have entered the first decade of the twenty-first century, we can cheaply purchase small personal computers (PCs) with the same capabilities as those of the mainframe computers of earlier decades. With advances in computer technology, Chinese characters can now be input directly as data. Many offices operating population-based cancer registries have changed their registration systems to take advantage of this advance.

In 2004, the Japan Cancer Surveillance Research Group (chaired by Dr. Tomotaka Sobue) introduced standard procedures for cancer registries in Japan by selecting a set of 25 standard items for every cancer registry to collect and a standard registry system based on a PC platform[17] (see Table 2)

Table 2. Changes in data items collected at cancer registries in Japan

Item collected	At beginning of cancer survey	At beginning of cancer registry	Standard items in standard registry
Name of hospital		O	O
Patient's ID no. in hospital		O	O
Patient's name	O	O	O
Sex	O	O	O
Age	O		
Birth date		O	O
Address of patient	O	O	O
Date of first symptom	O		
Diagnosis	O	O	O
Date of diagnosis		O	O
Site of cancer	O	O	
Laterality			O
Primary site			O
Histology		O	O
Extension of disease		O	O
Method of diagnosis	O	O	O
Screening or first symptoms		O	O
Surgery of primary site		O	O
Laparo/thoracoscopic surgery			O
Endoscopic surgery			O
Result of surgery			O
Date of surgery		O	O
Radiation therapy		O	O
Chemotherapy		O	O
Immunotherapy		O	O
Endocrine therapy			O
Other therapies		O	O
Date of death		O	O
Cause of death		O	
Place of death		O	

O, collected item

Protection of personal information and laws related to cancer registries

Notification of cancer cases to the population-based cancer registries in Japan is not compulsory for physicians and medical institutions, but voluntary. The Law on Health and Medical Services for the Aged enacted in 1983 was the first law to recommend that the prefectures establish cancer registries to help them with anti-cancer programs and to evaluate cancer-screening programs. The effects of this recommendation were obscure, however, and the law was withdrawn several years later. Though many provisions of this law were reintroduced in an amended law enacted in 1986, the provisions on cancer registries were dropped. Later, in 2003, population-based cancer registration was officially reintroduced as a voluntary task in the newly enacted Health Promotion Law. This law requires national and municipal governments to take steps to ascertain details of the onset of lifestyle-related diseases such as cancer and cardiovascular disease. The Cancer Control Act, approved in 2006, recognizes cancer registries as one of the most important axes of cancer control activities.

JACR and the Research Group for Cancer Registration published *Guidelines for confidentiality in the cancer registration scheme* in 1996[13] and have promoted the protection of personal information since then. The guidelines drew upon the IACR *Guidelines on confidentiality in cancer registries*. The Japanese version of these guidelines was revised in 2005. The guidelines recommend that the staff of population-based cancer registries carry out the registration tasks strictly, so as to avoid infringing upon individual rights or interests due to the loss, leakage, or other mishandling of personal information (see column headed "Laws, guidelines, conferences" in Table 1)

Current and future status of cancer registries in Japan

Though most registries in Japan are conducted by prefectural governments in cooperation with prefectural medical associations and cancer centers, central offices for cancer registration management have also been established by prefectural medical associations, cancer societies, cancer detection centers, centers for health promotion, medical universities, and prefectural governmental offices. The registration systems they use have not been constructed uniformly. According to the second questionnaire survey on the status of cancer registries, conducted in 2006, the proportion of death-certificate-only (DCO) cases averaged 35.4% and ranged from 0% to 100% (see Table 3 and Fig. 2).

The Third-Term 10-Year Comprehensive Strategy for Cancer Control program was commenced in 2004. Improved

Table 3. Current status of population-based cancer registries in Japan

Prefecture number	Prefecture name	Population[a]	Cancer incidence (number)	Cancer mortality (number)	DCN (%)	DCO (%)	IM ratio
1	Hokkaido	5683062	20265	14634	36.8	36.8	1.38
2	Aomori	1475728	6734	3968	45.9	45.9	1.70
3	Iwate	1416180	5878	3819	35.7	35.7	1.54
4	Miyagi	2365320	11832	5360	14.0	14.0	2.21
6	Yamagata	1239133	6817	3580	21.9	12.4	1.90
8	Ibaragi	2985676	10419	6942	37.9	34.3	1.50
9	Tochigi	2004817	7316	4633	41.3	41.3	1.58
10	Gunma	2024852	6145	4755	61.5	61.5	1.29
12	Chiba	5926349	19406	12503	36.6	31.8	1.55
14	Kanagawa	8489932	27598	17570	33.1	33.1	1.57
15	Niigata	2475733	12339	6757	20.5	20.5	1.83
16	Toyama	1120851	7191	3035	37.6	37.6	2.37
17	Ishikawa[b]	1180977	3232	2983	47.5	47.5	-
18	Fukui	828944	3723	2130	9.5	0.0	1.75
21	Gifu	2107700	6229	4918	45.2	45.2	1.27
23	Aichi	7043300	24600	14620	32.5	32.5	1.68
25	Shiga	1342832	5430	2836	26.7	15.8	1.91
26	Kyoto	2644391	7105	6602	30.6	30.6	1.08
27	Osaka	8805081	32007	21325	37.3	26.0	1.50
31	Tottori	613289	3286	1751	26.1	15.3	1.88
33	Okayama	1937571	10338	4912	16.3	7.6	2.10
34	Hiroshima	2878915	19015	7272	37.5	37.5	2.61
35	Yamaguchi	1527964	5977	4420	35.2	18.4	1.35
36	Tokushima	824108	2579	2260	80.8	80.8	1.14
37	Kagawa	1029073	1734	2723	100.0	100.0	0.64
38	Ehime	1493092	5694	3912	53.7	53.7	1.46
39	Kouchi	813946	2401	2286	60.3	47.8	1.05
41	Saga	876654	4172	2449	34.5	10.5	1.70
42	Nagasaki	1516523	8926	4264	10.8	10.8	2.09
43	Kumamoto	1854055	7790	4855	37.7	37.7	1.60
46	Kagoshima	1786194	6739	4914	73.1	73.1	1.37
47	Okinawa	1318220	3838	2411	37.6	37.6	1.59
–	Average	2488452	9586	5981	39.2	35.4	1.62

[a] Population in 2005 census
[b] Limited sites only

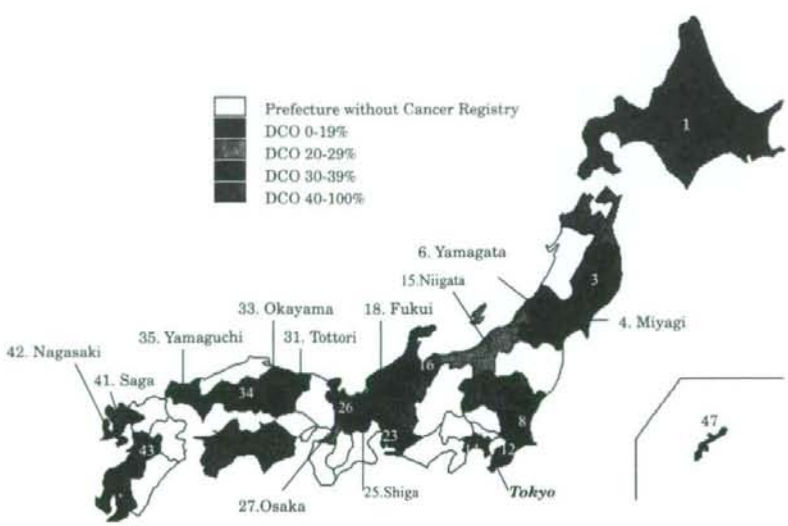

Fig. 2. Prefectures without cancer registries and percentages of death-certificate-only (DCO) cases by prefecture

data for cancer registries are essential for the assessment of cancer incidence, as cited by the program. To improve the quality of the data, the Japan Cancer Surveillance Research Group is now taking steps to standardize the procedures for population-based cancer registries. Though the standardization of population-based cancer registries has dramatically improved through the activities of this Research Group, there are still problems with cancer registries that must be solved soon. Because legal support is necessary, the JACR has issued a declaration requesting a legal basis for reporting to cancer registries through the enactment of a Cancer Registry Law (tentative name). There are hopes that this new law, if enacted, will markedly improve the proportions of DCN and DCO cases, and the incidence/mortality (IM) data in cancer registries in Japan.

Acknowledgments The author thanks Dr. Aya Hanai, Dr. Nobuo Nishi, Dr. Yoshi Okuno, and the late Dr. Akira Takano, for their advice and for their dissemination of limited copies of this paper.

References

1. Wager G (1991) History of cancer registration. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet RG (eds) Cancer registration principles and methods. IARC Scientific Publication no. 95. IARC, Lyon, pp 3–6
2. Segi M, Fukushima I, Mikami Y, et al. (1954) Cancer illness; among residents of Miyagi Prefecture, Japan, 1951. Tohoku J Exp Med 59:213–224
3. Segi M, Fukushima I, Fujisaki S, et al. (1957) Cancer morbidity in Miyagi Prefecture, Japan and a comparison with morbidity in the United States. J Natl Cancer Inst 18:373-383
4. Segi M, Fuzisaki S, Kurihara M (eds) (1960) Cancer in Japan and the world; epidemiology, statistics and geographical pathology of cancer. Shindan To Chiryo Sha, Tokyo
5. Segi M (1966) Japan, Miyagi Prefecture. In: Doll R, Payne P, Waterhouse J (eds) Cancer incidence in five continents, a technical report. Springer, Berlin Heidelberg Tokyo New York, pp 118–119
6. Aoki K, Kurihara M (1994) The history of cancer registration in Japan: contribution of Dr Mitsuo Segi. Cancer Surv 19:563–570
7. Monzen T, Wakabayashi T (1986) Tumor and tissue registries in Hiroshima and Nagasaki. Gann Monograph on Cancer Res, no. 32:29–40
8. Hanai A, Fujimoto I, Tsukuma H, Oshima A (1999) Cancer registration and cancer trends in Japan. In: Sato S, Miller MW, et al. (eds) Proceedings of the International Symposium "Cancer Epidemiology and Control in the Asia-Pacific Region." International Center for Medical Research, Kobe, pp 80–88
9. Haenszel W (1987) Segi M 1908–1982, Changing cancer pattern and topics in cancer epidemiology, in memory of Professor Mitsuo Segi. Japanese Cancer Association/Japan Scientific Societies, Tokyo; Plenum, New York
10. Fujimoto I (ed) (1975) Guidelines for population-based cancer registration in Japan (in Japanese). The Research Group for Population-Based Cancer Registration in Japan, Osaka
11. Shigematsu T, Yamasaki M, Hanai A, Sakagami F (eds) (1977) Standardized methods of population-based cancer registry (in Japanese). The Research Group for Population-Based Cancer Registration in Japan, Osaka
12. Hanai A, Oshima A (eds) (1999) Guidelines for population-based cancer registration in Japan (fourth revision; in Japanese). The Research Group for Population-Based Cancer Registration in Japan, Osaka
13. Tanaka H, et al. (eds) (1996) Guidelines for confidentiality in the cancer registration scheme (in Japanese). The Research Group for Population-Based Cancer Registration in Japan, Osaka
14. Hanai A, Fujimoto I (1993) Cancer registration in Osaka. Cancer incidence and mortality in Osaka, 1963–1989. Shinohara-Shuppan, Tokyo, pp 226–235
15. Oshima A, Sakagami F, Hanai A, Fujimoto I (1979) A method of record linkage. Environ Health Perspect 32:221–230
16. Fujimoto I, Hanai A, Oshima A, et al. (1984) Record linkage in the Osaka Cancer Registry and its application in cancer epidemiology. In: Blot WJ, Hirayama T, Hoel DG (eds) Statistical methods in cancer research. Gann (Suppl), Tokyo, pp 129–141
17. Sobue T, Tsukuma H, Okamoto N, Ajiki W (2007) Handbook on population-based cancer registration in Japan (fifth revision; in Japanese). The Japan Cancer Surveillance Research Group, Tokyo

doi:10.1111/j.1447-0756.2008.00738.x
J. Obstet. Gynaecol. Res. Vol. 34, No. 4: 543–551, August 2008

Anxiety and prevalence of psychiatric disorders among patients awaiting surgery for suspected ovarian cancer

Akiko Sukegawa[1], Etsuko Miyagi[1], Mikiko Asai-Sato[1], Haruya Saji[1], Ken Sugiura[1], Takehiko Matsumura[2], Atsushi Kamijyo[2], Yoshio Hirayasu[2], Naoyuki Okamoto[3] and Fumiki Hirahara[1]

Departments of [1]Obstetrics and Gynecology and [2]Psychiatry, Yokohama City University School of Medicine, [3]Division of Cancer Prevention and Cancer Control, Kanagawa Cancer Center Research Institute, Yokohama, Japan

Abstract

Aim: The goal of the current study was to determine the anxiety level and prevalence of psychiatric disorders among patients awaiting surgery for ovarian tumors. Also analyzed were the predictive factors for psychiatric disorders and changes after surgical diagnosis.

Methods: Patients who underwent surgery for ovarian tumors were examined before and after surgery with the MINI International Neuropsychiatric Interview, the Spielberger State-Trait Anxiety Inventory (STAI) and the Mausley Personality Inventory (MPI). Participants diagnosed with cancer were examined a third time after being given an explanation about whether or not adjuvant chemotherapy was required.

Results: Twenty-seven participants completed the study and were analyzed. Nine (33.3%) of these 27 participants were diagnosed as having adjustment disorder. There were no differences in the demographic data, STAI trait anxiety score and MPI score between the participants with or without adjustment disorder. At the pre-surgical interview, the STAI state anxiety score of the participants was high (49.5 ± 10.30). After pathological examination of the tumors, it was found that 12 patients had cancer (malignant group) and 15 patients had a benign tumor (benign group). At pre-surgery, the prevalence of adjustment disorder and the level of anxiety in the benign group were similar to those in the malignant group. There was a second surge of anxiety in patients who needed chemotherapy.

Conclusion: The above findings demonstrate that patients with suspected ovarian cancer experience a high level of anxiety. Physicians should be aware of the risk of adjustment disorder in these patients. Additionally, ovarian cancer patients need psychological assessment during the course of treatment.

Key words: adjustment disorder, anxiety, ovarian tumor, pre-surgery, psychiatric disorder.

Introduction

The incidence of psychiatric complications has been reported to be as high as 47% among patients with malignant tumors; 32% of these are adjustment disorders and 6% are depression.[1] Visser *et al.*[2] reported that the quality of life of newly diagnosed cancer patients waiting for surgery is seriously impaired compared with the general population. Patients with suspected malignant breast tumor who were subsequently diagnosed as having a benign tumor showed the same high pre-surgical potential for anxiety as patients who were subsequently diagnosed with breast cancer.[3] Onishi *et al.*[4] reported a case of post-traumatic stress disorder (PTSD) induced by the suspicion of lung cancer.

Across studies focusing on psychiatric distress in ovarian cancer patients, between 30 and 70% of ovarian cancer patients reported moderate to severe levels of

Received: July 30 2007.
Accepted: October 24 2007.
Reprint request to: Dr Etsuko Miyagi, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan.
Email: emiyagi@med.yokohama-cu.ac.jp

anxiety,[5-9] and one-fifth of patients reported symptoms suggestive of clinical depression.[10] A specific feature of ovarian tumors is the uncertainty of the pre-operative diagnosis. Ovarian tumors cannot be definitively differentiated as benign or malignant using a combination of ultrasonography, magnetic resonance imaging (MRI) and tumor markers for pre-surgical diagnosis. On the basis of intraoperative findings, surgical treatment becomes radical for ovarian cancer, but consists of only salpingo-oophorectomy for benign ovarian tumors. Thus, most ovarian tumor patients receive an indistinct explanation about their diagnosis and operation before their surgical procedure. In our experience, many ovarian tumor patients express anxiety or fear about the possibility of ovarian cancer in the interval before surgery. However, little research has focused on pre-surgical psychiatric complications and anxiety in patients with ovarian tumor.

Our objectives were to determine the level of anxiety and the prevalence of psychiatric disorders caused by the diagnosis of ovarian tumor in patients awaiting surgery. Additionally, the predictive factors for psychiatric disorders and post-surgical change when the patients received their diagnosis of cancer or benign tumor were statistically analyzed.

Methods

The present study was conducted prospectively in the Department of Obstetrics and Gynecology at Yokohama City University Hospital. Patients awaiting surgery for ovarian tumor were recruited to participate in this study. Inclusion criteria were surgery for ovarian tumor as the first treatment in which it was not known whether the tumor was benign or malignant, age from 20 to 80 years, ability to speak and read Japanese, and willingness to participate in the study after informed consent. We excluded the following patients: those with psychiatric complications, those diagnosed with ovarian cancer with positive cytological findings upon examination of the ascites, those scheduled for laparoscopic surgery or emergency surgery, those with poor Eastern Cooperative Oncology Group performance status[11] (ECOG PS 2 or higher), and those with confirmed pregnancy. Approval of this study was given by the Research Ethics Committee of Yokohama City University.

The patients received information about the study by way of an explanatory leaflet when they were scheduled for surgery at the outpatient clinic. Participants who gave written consent were interviewed one day before the surgery after they were hospitalized (Time 1 [T1]). Seven to 14 days after the first interview, depending on the patient's post-surgical condition, the patient was assessed again (Time 2 [T2]) after she received her preliminary diagnosis from her physician based on the intraoperative findings. Patients who were diagnosed as having cancer were interviewed a third time after an explanation of their final diagnosis, prognosis, and necessity of adjuvant chemotherapy or not (Time 3 [T3]) (Fig. 1).

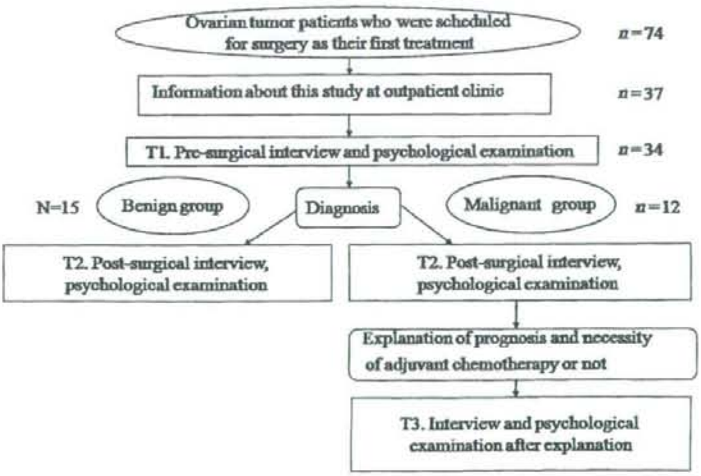

Figure 1 Flowchart of the present study. T1, first interview (pre-surgery); T2, second interview (post-surgery after confirmation of the preliminary diagnosis); T3, third interview (after the explanation about the prognosis and necessity of adjuvant chemotherapy or not).

All interviews were conducted in a private room by one researcher (A. S., a Japanese female gynecologist with psychiatric training). The first (T1) interview consisted of a semi-structured questionnaire, a structured interview to confirm whether the patient had any psychiatric disorders, and psychological examinations. The semi-structured questionnaire in the T1 interview focused on demographic data, such as past history, medical complications, marital status, perinatal history, familial history, education level, and employment status, in addition to data about the present condition, such as primary symptoms and emotional state at the time of the interviews. The second (T2) and third (T3) interviews focused on the same points as the T1 interview, except that they did not include demographic questions. Physiological data concerning the illness were collected from patients' medical records.

The structured interview in the T1, T2 and T3 interviews consisted of the MINI International Neuropsychiatric Interview, Japanese version 5.0.0 2003 (M.I.N.I.), to detect psychiatric disorders based on DSM-IV. To detect for adjustment disorder, we added four questions to the M.I.N.I. that were reported by Passik *et al.*[12] The abovementioned authors verified the validity of the M.I.N.I. with modifications for adjustment disorder as a way for medical staff other than psychiatrists to detect for psychiatric disorders including adjustment disorder.[12]

The psychological examination consisted of two self-reported questionnaires to assess the participants' psychological status. One of them was the Spielberger State-Trait Anxiety Inventory (STAI),[13] Japanese version,[14] which is a well-known 40-item instrument measuring both transient and enduring levels of anxiety. The cut-off score for state anxiety on the STAI of 42 was adopted based on the study that examined the validity of the STAI in Japanese women.[14] Also used was the Mausley Personality Inventory (MPI),[15] Japanese version.[16] The MPI is a personality inventory with 80 items developed by Eysenck,[15] and the reliability and validity of the Japanese version have been confirmed in Japanese people.[16] The MPI consists of 24 items measuring extroversion tendency (E scale), 24 items measuring neurotic tendency (N scale), 20 items measuring social desirability (lie; L scale), and 12 other items. The participants filled out these two questionnaires by themselves after the interviews in the same private room.

To clarify the relationship between the participants' anxiety and pre-surgical explanation, the participants' attending physicians were asked if they had explained to the patient before the surgery whether the probability of cancer was high, moderate or low. In our department, the physicians' explanation to ovarian tumor patients is generally based on a protocol for ovarian tumors where it is not known whether the tumor is benign or malignant. They explain that ovarian tumors cannot be definitively differentiated as benign or malignant before surgery. In addition, they tell the patient whether the probability of cancer is high, moderate or low based on the clinical examination.

We analyzed the data from two viewpoints. First, we analyzed whether the prevalence of psychiatric disorders depended on the ovarian tumor diagnosis and the level of anxiety in the preoperative interview (T1). We also analyzed the predictive factors for psychiatric disorders, including age, marital status, hope to preserve fertility, complications, history of surgery, educational level, employment status, familial history of cancer, primary symptoms of this illness, performance status at T1, serum tumor marker levels, and diameter of the tumor. Second, the participants were divided into the following two groups: the malignant group which consisted of patients who were subsequently diagnosed as having ovarian cancer, and the benign group, which consisted of patients who were subsequently diagnosed as having a benign tumor. We compared the rates of pre- and post-operative psychiatric disorder and anxiety level. Additionally, the malignant group was divided into the group of patients who were recommended to undergo chemotherapy and the group of patients who were recommended to undergo follow-up without chemotherapy, and we compared the anxiety level at T3.

Student's *t*-test was used to assess group differences in continuous variables; in cases of abnormal distribution, the Wilcoxon rank sum test was used. χ^2 test was used to assess group differences in categorical variables; in the case of small sample sizes, Fisher's exact test was used. All analyses were performed using SPSS version 11.0 for Windows (Chicago, IL, USA).

Results

Participants

Among the 151 patients who underwent surgery as the primary treatment for ovarian tumor between June 2005 and February 2007, 77 were excluded because of the exclusion criteria described in the Methods section above. Thirty-seven of the remaining 74 cases were informed of this study, and all except one patient consented to participate. However, two patients did not undergo the first interview because of emergency

Table 1 Prevalence of psychiatric disorder and State-Trait Anxiety Inventory state anxiety scores at pre-surgery

Prevalence of psychiatric disorder ($n = 27$)	
Adjustment disorder	33.3% (9 cases)
Non-adjustment disorder†	66.7% (18 cases)
STAI state anxiety score (mean ± SD) ($n = 27$)	49.5 ± 10.30
Over cut-off point (≥42)	77.8% (21 cases)
Under cut-off point (42<)	22.2% (6 cases)

†Diagnosed as having no psychiatric disorder.

surgery or worsening of general condition (ECOG PS 2). Seven other patients did not complete the interviews for the following reasons: being diagnosed as having no gynecological cancer (four cases), not filling out the psychological questionnaires (one case), and being diagnosed previously with panic disorder (two cases). Therefore, 27 patients were processed and analyzed.

Prevalence of psychiatric disorders and anxiety among pre-surgical ovarian tumor patients

Nine (33.3%) of these 27 participants were diagnosed as having adjustment disorder by the M.I.N.I. with modifications. There was no other diagnosis of psychiatric disorders among the participants in this study (Table 1). The mean STAI state anxiety score of the 27 patients was higher than the average score among Japanese women in the general population (49.5 ± 10.30 *vs* 36.6 ± 9.06), with 21 participants (77.8%) having a score over the cut-off point (Table 1). Twenty-two participants (81.5%) reported feeling anxiety prior to the surgery because of the following reasons: possibility of cancer (20 cases); possible complications of surgery (11 cases); change in the patient's life after surgery (eight cases); concern for her family (three cases); preoperative physical symptoms such as pain due to the ovarian tumor (two cases); and concern for their job (two cases). The demographic data and physical symptoms in the adjustment disorder group ($n = 9$) were compared with those in the non-adjustment disorder group ($n = 18$) (Table 2). There were no significant differences in the demographic and medical characteristics between the two groups. Neither the STAI trait anxiety score nor the MPI score was related to the presence of psychiatric disorder. The STAI state anxiety score was significantly higher in the adjustment disorder group than in the non-adjustment disorder group (56.9 ± 7.72 *vs* 45.9 ± 9.55; $P = 0.006$) (Table 3). The proportions of patients to whom the physicians stated that the patient had a low, moderate or high probability of having ovarian cancer did not significantly differ between the two groups.

Post-surgical alteration in the malignant and benign groups

Among the 27 participants, 12 participants were diagnosed with gynecological cancer (including one participant with endometrial cancer with ovarian metastasis) and 15 participants were diagnosed with benign ovarian or para-ovarian cysts. The demographic data of the malignant and benign groups were similar (data not shown). The majority of participants (11/12 cases) in the malignant group had primary symptoms of ovarian tumor, in contrast to seven of the 15 patients in the benign group ($P = 0.047$). As to the explanation before surgery, the physician described the probability of cancer as moderate or high to all participants in the malignant group; in contrast, the physician described the risk of cancer as low to six of the 15 patients in the benign group (Table 4). In the malignant group and benign group, the prevalence of adjustment disorder at T1 was 50.0% (6/12) and 20.0% (3/15), respectively ($P = 0.199$; Fig. 2). Post-operatively (T2), the prevalence of adjustment disorder changed to 41.7 and 6.7%, respectively ($P = 0.083$). One notable finding was that four of the six participants who had been diagnosed with adjustment disorder in the malignant group before surgery recovered from the adjustment disorder when they received their diagnosis (T2). Three patients in the malignant group were newly diagnosed as having adjustment disorder post-surgery (T2). The malignant group was more prone than the benign group to suffer from adjustment disorder both before and after surgery, although no significant difference was detected between the two groups.

The STAI trait anxiety score and the scores on the three scales of MPI were analyzed as a percentage of the respective score at T1. The STAI trait anxiety score of the malignant group did not change from T1 to T3; however, in the benign group the score decreased significantly ($P = 0.003$) at T2 (Fig. 3a). The scores on the three scales of the MPI did not significantly change during the study in each group (Fig. 3b). The STAI state anxiety score at T1 was 50.1 ± 10.72 and 49.1 ± 10.31 in the malignant and benign groups, respectively (Fig. 4). However, the mean score of the benign group at T1 was unexpectedly high and was above the cut-off point. The mean STAI state anxiety score of the malignant group

Table 2 Demographic and medical characteristics of the adjustment disorder and non-adjustment disorder groups

	Adjustment disorder group ($n = 9$)	Non-adjustment disorder group ($n = 18$)
Age (mean ± SD, years)	50.1 ± 15.7	51.0 ± 15.3
Living with husband	7 (77.8%)	13 (72.2%)
Hope for fertility	2 (22.2%)	4 (22.2%)
Complications	5 (55.6%)	9 (50.0%)
Past history of surgery	4 (44.4%)	7 (38.9%)
Education beyond high school	4 (44.4%)	10 (55.5%)
Employment	6 (66.6%)	13 (72.2%)
Familial history of cancer	6 (66.7%)	10 (55.5%)
Physical symptoms at first visit	6 (66.7%)	11 (61.1%)
Performance status 0	7 (77.8%)	15 (83.3%)
Performance status 1	2 (22.2%)	3 (16.7%)
Mean diameter of ovarian tumor	8.5 ± 3.9 cm	9.1 ± 3.5 cm
Rising levels of tumor markers	4 (44.4%)	13 (72.2%)

There were no significant differences in any of the characteristics between the adjustment disorder and non-adjustment disorder groups.

Table 3 State-Trait Anxiety Inventory/Mausley Personality Inventory (STAI/MPI) results and explanation in the adjustment disorder and non-adjustment disorder groups at pre-surgery (Time 1)

	Adjustment disorder group ($n = 9$)	Non-adjustment disorder group ($n = 18$)
STAI trait anxiety score	38.6 ± 6.42	36.6 ± 5.57
STAI state anxiety score†	56.9 ± 7.72	45.9 ± 9.55
MPI extroversion scale	33.1 ± 6.99	28.4 ± 10.22
MPI neuroticism scale	11.3 ± 6.08	6.7 ± 6.54
MPI lie scale	16.7 ± 4.80	18.8 ± 6.04
Probability of cancer‡ (moderate or high)	9 (100%)	12 (66.7%)

†The STAI state anxiety score in the adjustment disorder group was significantly higher than in the non-adjustment disorder group ($P = 0.006$); ‡degree of probability of cancer mentioned by physicians in the preoperative explanation of the probability of cancer to the patient.

Table 4 State-Trait Anxiety Inventory (STAI) state anxiety scores and explanation in the malignant and benign groups at pre-surgery (Time 1)

	Malignant group ($n = 12$)	Benign group ($n = 15$)
STAI state anxiety score	50.1 ± 10.72	49.1 ± 10.31
Probability of cancer† (moderate or high)	12 (100.0%)	9 (60.0%)

†Degree of probability of cancer mentioned by physicians in the preoperative explanation of the probability of cancer.

remained above the cut-off point at T2 (43.2 ± 11.37). However, the score significantly decreased at T3 ($P = 0.044$) because some participants reported that they felt that they were free from cancer as a result of the surgery, or they were prepared to fight against cancer after the cancer diagnosis was clarified. At T3, the mean score of the seven participants who were recommended to undergo chemotherapy was high (50.2 ± 11.43) because they had received the explanation about adjuvant chemotherapy and the risk of

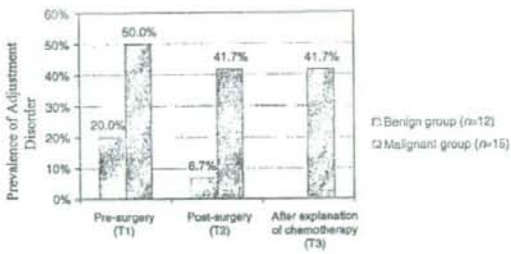

Figure 2 Prevalence of adjustment disorder in the malignant and benign groups at times T1, T2 and T3. The prevalence of adjustment disorder in the malignant group tended to be higher than that in the benign group at T2.

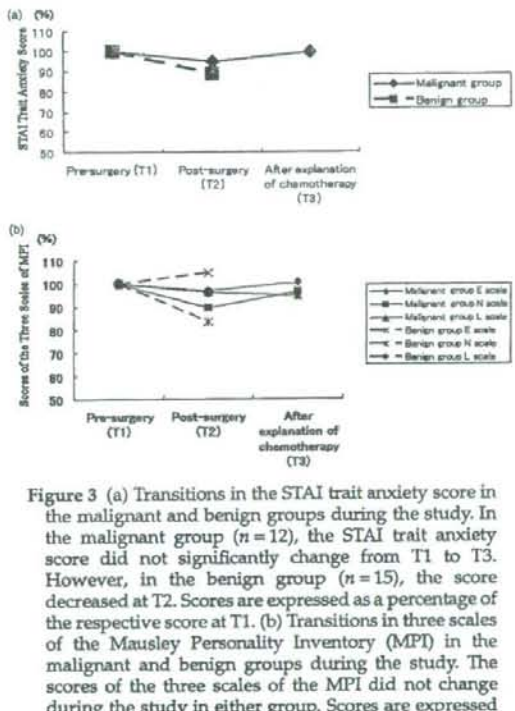

Figure 3 (a) Transitions in the STAI trait anxiety score in the malignant and benign groups during the study. In the malignant group ($n = 12$), the STAI trait anxiety score did not significantly change from T1 to T3. However, in the benign group ($n = 15$), the score decreased at T2. Scores are expressed as a percentage of the respective score at T1. (b) Transitions in three scales of the Mausley Personality Inventory (MPI) in the malignant and benign groups during the study. The scores of the three scales of the MPI did not change during the study in either group. Scores are expressed as a percentage of the respective score at T1. (Malignant group $n = 12$; benign group $n = 15$).

recurrence. In contrast, the mean level of anxiety in the five participants who were not recommended to undergo chemotherapy in the malignant group decreased slightly (38.8 ± 14.27) because the status of

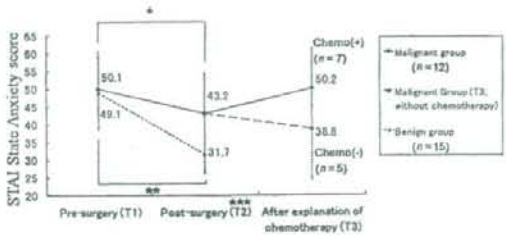

Figure 4 Transitions of the STAI state anxiety score of the malignant and benign groups during the study. *In the malignant group, the STAI state anxiety score at T2 was significantly lower than that at T1, although it remained above the cut-off point (43.2 ± 11.37; $P = 0.043$). **In the benign group, the STAI state anxiety score decreased immediately after the patients were told that their tumors were benign ($P = 0.000007$). ***At pre-surgery (T1), the STAI state anxiety score of the benign group did not significantly differ from that of the malignant group. However, at post-surgery (T2), the STAI state anxiety score of the benign group became significantly lower than that of the malignant group ($P = 0.005$).

cancer was not as bad as they had expected. After the surgery, the STAI state anxiety score of the benign group decreased immediately (T2, 31.7 ± 5.32; $P = 0.000007$) and fell below the cut-off point. At T2, the STAI state anxiety score of the benign group was significantly lower than that of the malignant group ($P = 0.005$).

Discussion

Anxiety and psychological distress among ovarian cancer patients have been reported in several studies, but little research into the prevalence of psychiatric disorders diagnosed by DSM-IV[17] has been carried out among pre-surgical ovarian tumor patients. In the present study, adjustment disorder was diagnosed in one-third (9/27) of suspected ovarian cancer patients waiting for primary surgery. This prevalence is similar to the rate of adjustment disorder among general cancer patients (32%) reported by Derogatis *et al.*[1] Before the surgery (T1), the STAI state anxiety score of the 27 participants was high (49.5 ± 10.30). One of the influential factors that increased the level of anxiety was the fear of surgery. In addition, the possibility of ovarian cancer might affect the pre-surgical anxiety. Lalinec-Michaud and Engelsmann[18] examined 102 women undergoing hysterectomy for reasons other than cancer, and their mean pre-operative STAI state anxiety score was 41.6. Kindler *et al.*[19] examined 734 patients one day before surgery, and their mean score was 39.0. Iwata *et al.*[20] examined 51 women just before surgery for varicose veins with local anesthesia, and their mean score was 45.6. In the present study, many participants (21/27 cases) reported that one of the causes of pre-surgical anxiety was the possibility of cancer. The STAI state anxiety score in this study was higher than in previous reports, indicating that fear of the possibility of ovarian cancer worsens pre-surgical anxiety.

The following specific risk factors related to psychological distress in ovarian cancer patients have been reported: young age,[8,9] progression of carcinoma, recurrence of tumor, short time from cancer diagnosis,[8] poor social support, history of physical disease and psychiatric disorders.[9] We assessed predictive factors, such as demographic data and the patients' character, but these did not predict adjustment disorder. The STAI trait anxiety score and MPI-N scale tended to be higher in the adjustment disorder group than the non-adjustment disorder group; however, these differences were not statistically significant. Although these results were in part due to the sample size, adjustment disorder might be difficult to predict by demographic factors or the participants' character, as has been previously reported. Further research is needed to elucidate the predictive factors for adjustment disorder. The probability of cancer mentioned in the pre-surgical explanation did not impact on the prevalence of adjustment disorder. Donovan *et al.*[21] reported that patient-provider communication affected symptom control in ovarian cancer patients. Although it cannot be denied that each patient–gynecologist relationship affects the patients' anxiety, the patient–gynecologist relationship in the current study was not evaluated by quantitative analysis. However, the attending physicians carefully explained to the participants based on the protocol before surgery, and most participants commented in the interviews on the kindness of their attending physicians. Both specific information about their disease and emotional support were reported to be necessary to reduce patients' psychological distress for cancer patients,[22,23] including ovarian[24,25] and cervical[26–28] cancer patients. Mishel[29] reported that uncertainty about their condition affects the patients' anxiety. In pre-surgical counseling of ovarian tumor patients, the explanation included uncertainty and vagueness about the cancer, because it is not possible to clearly determine whether or not the tumor is malignant. Patients' anxiety may be amplified more by this uncertainty than by the level of severity mentioned in the explanation of the probability of cancer before surgery for ovarian tumors. In the current study, it is notable that two-thirds of the participants recovered from adjustment disorder when they received their cancer diagnosis after surgery.

In the present study, the prevalence of adjustment disorder prior to the surgery among the patients who were finally diagnosed as having a benign tumor was similar to that among the malignant group. The participants reported that the possibility of cancer made them anxious; therefore, the adjustment disorder developed due to anxiety or fear of the possibility of cancer. McGovern *et al.*[30] described that patients who received false-positive results on the cancer screening test had emotional and health distress and felt a lower quality of life. In addition, many participants reported that they were shocked when they first heard that they had an ovarian tumor in the outpatient clinic. Patients who are found to have an ovarian tumor might have a high level of anxiety more than one day before the surgery. We must attend to the psychological distress of patients from the time of detection of ovarian tumors.

The mean STAI state anxiety score after surgery in the malignant group was higher than that in the benign group. In the benign group, the mean STAI state anxiety score decreased immediately after the patients learned that their tumor was benign. The majority of patients who were finally found to have ovarian cancer were diagnosed as having adjustment disorder (9/12 cases). The period of this study extended from shortly before surgery to just after surgery and before adjuvant chemotherapy was started. However, cancer patients were reported to be at risk for developing severe psychiatric disorders, such as depression[1,10] or PTSD[31] during or after their treatment. In the present study, patients who were diagnosed with ovarian cancer received an explanation about their cancer diagnosis, the necessity of chemotherapy and the risk of recurrence. Therefore, the object of their anxiety changed with the progression of the cancer. The ovarian cancer patients continued to feel anxiety throughout their lives, especially those patients who received adjuvant chemotherapy. We previously reported two ovarian cancer patients who developed PTSD after being diagnosed with ovarian cancer.[32] It may seem that this adjustment disorder is not as severe as other psychiatric disorders, such as depression and PTSD, but Cuijpers and Smit[33] reported that sub-threshold depression (patients with clinically relevant depressive symptoms, without meeting the criteria for a fullblown major depressive disorder) is a risk factor for major depressive disorders. Therefore, patients who are diagnosed with adjustment disorder, especially those who are confirmed to have ovarian cancer, must be followed up intensively with regard to the progression of their psychological distress or psychiatric symptoms.

In this study, we showed that ovarian tumor patients awaiting surgery have a high level of anxiety. It is important to provide patients with pre-surgical information about their ovarian tumor, but we must deliberate on how to inform patients of the probability of ovarian cancer. However, in the present study, measurement of the severity of pre-surgical explanation was based on the attending physicians' report, and the quality or quantity of explanation may have been different for each physician; therefore, additional research is required to replicate this effort with objective measurement of the physicians' explanation.

In conclusion, we should consider and carefully monitor the psychiatric condition of patients during treatment of ovarian tumors, even in patients with benign disease. In ovarian cancer patients, especially those with adjustment disorder, long-term psychological follow-up is crucial.

Acknowledgments

We thank Hideki Onishi MD PhD for his support of the protocol of this study and Kikuko Miyazaki PhD for her assistance in performing the analyses in this study.

References

1. Derogatis LR, Morrow GR, Fetting J. The prevalence of psychiatric disorders among cancer patients. *JAMA* 1983; **249**: 751–757.
2. Visser MRM, Van Lanschot JJB, Van Der Velden J. Quality of life in newly diagnosed cancer patients waiting for surgery is seriously impaired. *J Surg Oncol* 2006; **93**: 571–577.
3. Neuhaus W, Zok C, Göhring UJ. A prospective study concerning psychological characteristics of patients with breast cancer. *Arch Gynecol Obstet* 1994; **225**: 201–209.
4. Onishi H, Onose M, Yamada T. Post-traumatic stress disorder associated with suspected lung cancer and bereavement: 4-year follow-up and review of the literature. *Support Care Cancer* 2003; **11**: 123–125.
5. Kornblith AB, Thaler HT, Wong G. Quality of life of women with ovarian cancer. *Gynecol Oncol* 1995; **59**: 231–242.
6. Portenoy RK, Kornblith AB, Wong G. Pain in ovarian cancer patients. *Cancer* 1994; **74**: 907–915.
7. Portenoy RK, Thaler HT, Kornblith AB. Symptom prevalence, characteristics and distress in a cancer population. *Qual Life Res* 1994; **3**: 183–189.
8. Norton TR, Manne SL, Rubin S. Prevalence and predictors of psychological distress among women with ovarian cancer. *J Clin Oncol* 2004; **22**: 919–926.
9. Hipkins J, Whitworth M, Tarrier N. Social support, anxiety and depression after chemotherapy for ovarian cancer: A prospective study. *Br J Health Psychol* 2004; **9**: 569–581.
10. Bodurka-Bevers D, Basen-Engquist K, Carmack CL. Depression, anxiety, and quality of life in patients with epithelial ovarian cancer. *Gynecol Oncol* 2000; **78**: 302–308.
11. Oken MM, Creech RH, Tormey DC. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982; **5**: 649–655.
12. Passik SD, Donaghy KB, Theobald DE. Oncology staff recognition of depressive symptoms on videotaped interviews of depressed cancer patients: Implications for designing a training program. *J Pain Symptom Manage* 2000; **19**: 329–338.
13. Spielberger CD, Goursh RL, Lushene RD. *STAI: Manual for the Sate -Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologist Press, 1970.
14. Mizuguchi T, Shimonaka Y, Nakazato K. *State-Trait Anxiety Inventory Handbook*. Kyoto: Sankyobou, 1991. (In Japanese.)
15. Eysenck HJ. *The Maudsley Personality Inventory*. London: University of London Press, 1956.
16. MPI Research Association. *New Personality Inventory; Maudsley Personality Inventory*. Tokyo: Seishin-Shobou, 1969. (In Japanese.)
17. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn. Washington, DC: American Psychiatric Press, 1994.
18. Lalinec-Michaud M, Engelsmann F. Anxiety, fears and depression related to hysterectomy. *Can J Psychiatry* 1985; **30**: 44–47.
19. Kindler CH, Harms C, Amsler F. The visual analog scale allows effective measurement of preoperative anxiety and detection of patients' anesthetic concerns. *Anesth Analg* 2000; **90**: 706–712.
20. Iwata H, Hirai M, Nukumizu Y. Change of psychological state in patients with Varicose Veins. *Jpn J Phlebol* 2004; **15**: 333–338. (In Japanese.)
21. Donovan HS, Hartenbach EM, Method MW. Patient-provider communication and perceived control for women experiencing multiple symptoms associated with ovarian cancer. *Gynecol Oncol* 2005; **99**: 404–411.
22. Schofield PE, Butow PN, Thompson JF. Psychological responses of patients receiving a diagnosis of cancer. *Ann Oncol* 2003; **14**: 48–56.
23. Randall TC, Wearn AM. Receiving bad news: Patients with haematological cancer reflect upon their experience. *Palliat Med* 2005; **19**: 594–601.
24. Parker PA, Kudelka A, Basen-Engquist K. The association between knowledge, CA125 preoccupation, and distress in women with epithelial ovarian cancers. *Gynecol Oncol* 2006; **100**: 495–500.
25. Stewart DE, Wong F, Cheung AM. Information needs and decisional preferences among women with ovarian cancer. *Gynecol Oncol* 2000; **77**: 357–361.
26. Hawighorst S, Schoenefuss G, Fusshoeller C. The physician-patient relationship before cancer treatment: A prospective longitudinal study. *Gynecol Oncol* 2004; **94**: 93–97.
27. Le T, Hopkins L, Menard C. Psychological morbidities prior to loop electrosurgical excision procedure in the treatment of

cervical intraepithelial neoplasia. *Int J Gynecol Cancer* 2006; **16**: 1089–1093.
28. De Groot JM, Mah K, Fyles A. The psychological impact of cervical cancer among affected women and their partners. *Int J Gynecol Cancer* 2005; **15**: 918–925.
29. Mishel MH. The measurement of uncertainty in illness. *Nurs Res* 1981; **30**: 258–263.
30. McGovern PM, Gross CR, Krueger RA. False-positive cancer screens and health-related quality of life. *Cancer Nurs* 2004; **27**: 347–352.
31. Smith MY, Redd WH, Peyser C. Post-traumatic stress disorder in cancer: A review. *Psychooncology* 1999; **8**: 521–537.
32. Sukegawa A, Miyagi E, Suzuki R. Post-traumatic stress disorder in patients with gynecologic cancers. *J Obstet Gynaecol Res* 2006; **32**: 349–353.
33. Cuijpers P, Smit F. Subthreshold depression as a risk indicator for major depressive disorder: A systematic review of prospective studies. *Acta Psychiatr Scand* 2004; **109**: 325–331.

Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 2, pp. 456–466, 2008

0360-3016/08/$–see front matter

doi:10.1016/j.ijrobp.2008.01.004

REDUCTION OF PROSTATE MOTION BY REMOVAL OF GAS IN RECTUM DURING RADIOTHERAPY

ICHIRO OGINO, M.D.,* HIROJI UEMURA, M.D.,[†] TOMIO INOUE, M.D.,[‡] YOSHINOBU KUBOTA, M.D.,[†] KAZUTO NOMURA, R.T.T.,[‡] AND NAOYUKI OKAMOTO, M.D.[§]

*Department of Radiation Oncology, Yokohama City University Medical Center, Yokohama, Japan; Departments of [†]Urology and [‡]Radiology, Yokohama City University Hospital, Yokohama, Japan; and [§]Department of Epidemiology, Kanagawa Cancer Center, Yokohama, Japan

Purpose: To evaluate the prostate and seminal vesicle motion in patients during both simulation and radiotherapy by rectal gas removal.

Methods and Materials: A total of 34 patients were treated in a whole pelvic radiotherapy (WPRT) arm and 42 patients in a non-WPRT arm. Of the 76 patients, 42 (26 in the non-WPRT arm and 16 in the WPRT arm) were instructed to insert their index finger and wash their rectums to evacuate their rectal gas. In addition to the planning computed tomography scan, three subsequent computed tomography scans were obtained during RT. The organs were outlined on each computed tomography image. Changes in the position of the prostate and seminal vesicles were analyzed using the center of mass (COM) coordinate system. The time trend, overall variations, systematic variations, and random variations were analyzed.

Results: The average cross-sectional area in the rectal gas removal group was significantly smaller than in all patients and in the WPRT arm. The vector of the prostate and seminal vesicle displacement for the rectal gas removal group was significantly smaller than in all patients. With rectal gas removal, the 95% confidence limit of the prostate displacement vector was reduced by 2.3 mm in the non-WPRT arm and 2.9 mm in the WPRT arm. The 95% confidence limit of the seminal vesicle displacement vector was reduced by 0.3 mm in the non-WPRT arm and 4.4 mm in the WPRT arm.

Conclusions: Using rectal gas removal, the cross-sectional area could be decreased, resulting in reduced motion and margins for the prostate and seminal vesicles. This is especially important for WPRT patients who require RT to the prostate, seminal vesicles, and pelvic lymph nodes. © 2008 Elsevier Inc.

Prostate cancer, Rectum, Motion, Whole pelvic radiotherapy, Average cross-sectional area.

INTRODUCTION

Image-guided radiotherapy (RT) has been increasingly used to aid in precise dose delivery to the target while reducing margins. These image-guidance methods for prostate localization include daily abdominal ultrasonography (1, 2), cone-beam computed tomography (CT) (3), fiducial markers (4, 5), and the rectal balloon (6). Radiopaque marker implants require invasive procedures. In addition, the markers can migrate and are implanted only in the prostate gland and not in the seminal vesicles. The images obtained by manual delineation of contours from cone-beam CT and interactive alignment by ultrasonography still contain uncertainty and are time-consuming. At present, these methods are not available in many RT facilities and require additional investigation.

Concern also exists about the motion of more than one organ. The Radiation Therapy Oncology Group 94-13 trial results demonstrated that total androgen suppression and whole pelvic RT (WPRT) followed by a prostate boost yielded better progression-free survival compared with total androgen suppression and RT to the prostate and seminal vesicles in patients with an estimated risk of pelvic lymph node (PLN) involvement of >15% (7, 8). To date, no data have been available about the motion of PLN. If the PLNs do not move relative to the prostate, either the PLN or prostate movement cannot be corrected by image-guided RT in patients undergoing WPRT.

Laxatives and enemas have been used to minimize rectal filling, variations in rectal volume, and motion of the prostate (9–11). Because many patients with WPRT present with diarrhea, it is not practical to use laxatives and enemas with these patients. We asked patients to evacuate their rectal gas by inserting their index finger and washing the rectum

Reprints requests to: Ichiro Ogino, M.D., Department of Radiation Oncology, Yokohama City University Medical Center, 4-57 Urafune-cho, Minami-ku, Yokohama 232-0024, Japan. Tel: (+81) 45-261-5656; Fax: (+81) 45-253-9955; E-mail: oginolro@urahp.yokohama-cu.ac.jp

Supported by the Yokohama Foundation for Advancement of Medical Science.

Conflict of interest: none.

Received Sept 4, 2007, and in revised form Dec 15, 2007. Accepted for publication Jan 5, 2008.

using a bidet-style toilet. The goal of this study was to evaluate the prostate and seminal vesicle motion in patients during both simulation and RT by rectal gas removal. We investigated patients in two treatment arms: non-WPRT and WPRT.

METHODS AND MATERIALS

Patients and treatment protocol

We investigated 76 prostate cancer patients treated with definitive RT between December 2004 and November 2006 at Yokohama City University Hospital.

The patients with an estimated risk of PLN involvement of >15% were treated with WPRT. The 34 patients in the WPRT arm were treated with 45 Gy to the PLNs using four-field three-dimensional conformal RT and then a boost to 77 Gy in the prostate and proximal seminal vesicles using intensity-modulated RT. The 42 patients in the non-WPRT arm received a prescribe dose of 50 Gy to the prostate and seminal vesicles and then a boost to 78 Gy to the prostate and proximal seminal vesicles using intensity-modulated RT. For the WPRT field, the vessels plus a 1.5-cm margin were used to define the common, external, and internal iliac nodal regions to the level of the L5–S1 interspace. To boost the prostate and proximal seminal vesicles, a 0.8-cm margin in the posterior direction and 1.0-cm margin in the other directions were used to define the planning target volume (PTV). All but 6 patients in the non-WPRT arm underwent neoadjuvant and concurrent hormonal therapy. The neoadjuvant hormonal therapy was started >3 months before RT.

Rectal gas removal

All patients were asked to urinate and defecate before treatment planning and each daily RT session. Special instructions were given to 42 patients (26 patients in the non-WPRT arm and 16 patients in the WPRT arm) to evacuate their rectal gas (Fig. 1). They were instructed to wear disposal gloves and smear olive oil on their index finger (Fig. 2a). They then inserted the index finger into the anus to widen the rectal canal and evacuate any rectal gas. The rectum was also washed with a cleansing jet of water to evacuate the rectal gas by a washlet (Toto USA, Morrow, GA) bidet-style toilet (Fig. 2b). These procedures were performed before CT and RT.

CT scans

All patients underwent CT in the supine position in an individualized commercialized thermoplastic cast from the abdomen to the thigh, with immobilization of the calf and ankles using Styrofoam to prevent rotation. In addition to the planning CT scan, three additional CT scans were obtained in the third week, the fifth week (before boost), and in the seventh week of the treatment course. These three scans (CT2–4), referred to as the treatment scans, were assumed to be representative of the patient's position during the treatment course. The repeat CT scans were made within 10

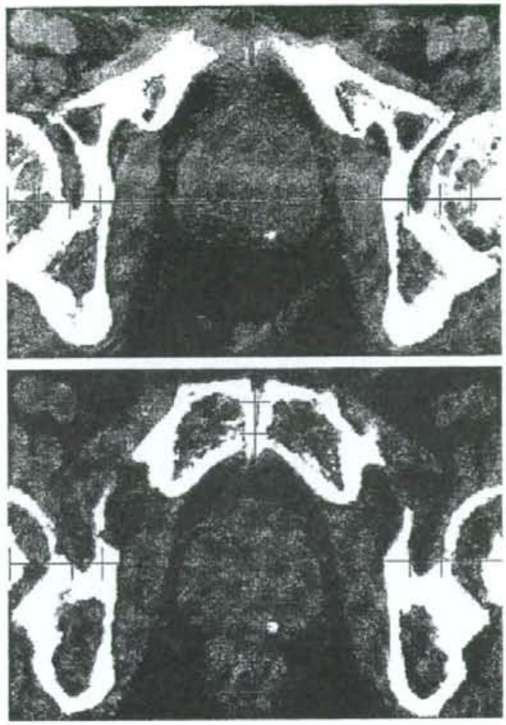

Fig. 1. Two transverse computed tomography scan slices taken on same day before gas removal (above) and after gas removal (below), demonstrating example of prostate movement resulting from extreme distension of unstable rectal gas. Prostate was displaced 1.2 cm posteriorly after gas removal.

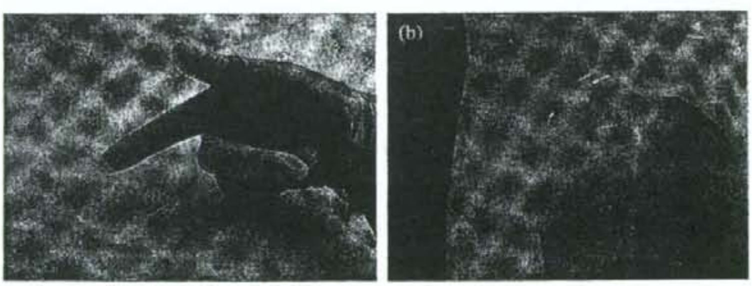

Fig. 2. (a) Rectal gas removal was achieved by inserting patient's index finger into anus to widen rectal canal. Patients wore disposal gloves, and olive oil was smeared on index finger. (b) Rectum was washed with cleansing jet of water using bidet-style toilet.

minutes after treatment delivery. The planning CT scan and CT scans during the treatment course were performed between 2 and 4 PM, and RT was usually delivered at the same time. A Toshiba multislice CT scanner was used, and the images were taken with a 3-mm-thick slice from the top of the fifth lumbar vertebra to 5 cm under the ischial tuberosities. No patients needed to undergo repeat CT scanning because of a large rectal volume.

Organ motion

The CT data were transferred to a commercially available treatment planning system (iXio, CMS, St. Louis, MO). The prostate, seminal vesicles, rectum, and bladder were contoured on all CT scans for each patient by 1 observer (I.O.). To outline the soft-tissue volumes consistently and correctly, in particular at the apex of the prostate, base of the prostate, and proximal seminal vesicles, we compared magnetic resonance imaging scans obtained with the individualized thermoplastic casts 15 min after the planning CT scan. The superior and inferior margins of the rectum were defined to be 1.5 cm above and 1.5 cm below the prostate volume. The average cross-sectional area (CSA), the rectal volume divided by the rectal length, was also calculated (12). The bladder was defined as the whole volume, including the cavity.

The treatment CT scans of each patient were matched with the planning CT scan by aligning the bony anatomy of the pelvic ring. Therefore, any setup error was assumed to have been removed. The center of mass (COM) was determined in the X (left–right), Y (superoinferior), and Z (anteroposterior) coordinate system. Changes in the position of the prostate and seminal vesicles were analyzed using changes in the COM coordinates system separately. For statistical comparison, the deviation in three directions from the initial treatment planning CT scan was also converted to a single vector ($\sqrt{\Delta X^2 + \Delta Y^2 + \Delta Z^2}$). The magnitude of this vector was used to describe the distance of the prostate and seminal vesicle COM displacement from the initial treatment planning CT scan. Because a large number of parameters make the analysis unnecessarily complicated and difficult to understand, we chose the COM in our model. The overall mean deviation M was the average value for all fractions and all patients. The overall standard deviation was the standard deviation (SD) value for all fractions and all patients. The random variation (σ) was defined as the SD of the day-to-day organ motion, averaged for all patients in the group. The systematic variations (Σ) was defined as the SD of the distribution of average organ deviations per patient in the group of patients (10).

Statistical analysis

The influence of rectal gas removal in the RT course was calculated using a repeated measures analysis of variance (ANOVA) test. In addition to ANOVA, the overall vector with and without rectal gas removal was compared using the *t* test. The *p* values given for the overall variations, systematic variations, and random variations were the results of F tests comparing the deviations with and without rectal gas removal. Factors with a difference at the $p = 0.05$ level were considered significant. The statistics were analyzed using Statistical Package for Social Sciences, version 11.0 (SPSS, Chicago, IL).

RESULTS

The influence of rectal removal in the RT course was calculated using a repeated measures ANOVA test. The prostate vector (mean ± SD, 4.4 ± 2.6), seminal vesicle vector (mean, 5.9 ± 3.1 mm), rectal volume (mean, 37.8 ± 12.6 cm^3), CSA (mean, 6.1 ± 2.1 cm^2), rectal volume changes (mean, 0.3 ± 13.2 cm^3), bladder volume (mean, 97.8 ± 52.4 cm^3), and bladder volume changes (mean, −18.4 ± 62.6 cm^3) were analyzed in all patients in the non-WPRT and WPRT arms. The effectiveness of rectal gas removal

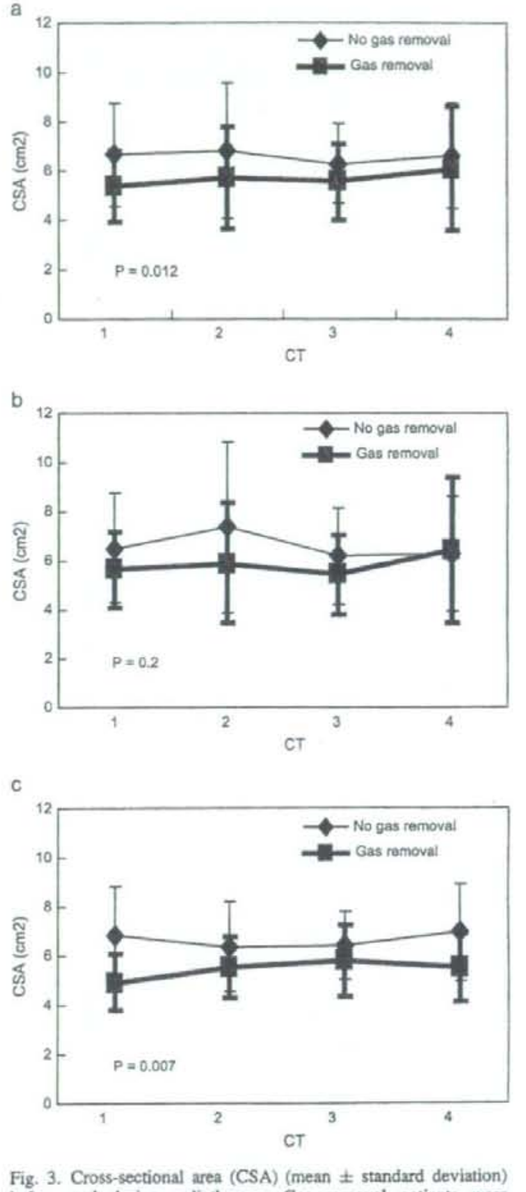

Fig. 3. Cross-sectional area (CSA) (mean ± standard deviation) before and during radiotherapy. Gas removal patients were compared with non–gas removal patients. (a) All patients. (b) Non-whole pelvic radiotherapy arm. (c) Whole pelvis radiotherapy arm. CT = computed tomography.

was not significant in terms of rectal volume, rectal volume changes, bladder volume, or bladder volume changes in all patients or stratified by the non-WPRT arm and WPRT arm.

The results of the CSA with or without gas removal are displayed in Fig. 3. No time trend was found with ANOVA. The CSA in the rectal gas removal patients was significantly smaller in all patients ($p = 0.012$) and in the WPRT arm ($p = 0.007$), but not in the non-WPRT arm ($p = 0.2$) by ANOVA (Fig. 3). The CSA on the planning CT scan was <9 cm^2 in all 42 patients who performed gas removal. During RT, the

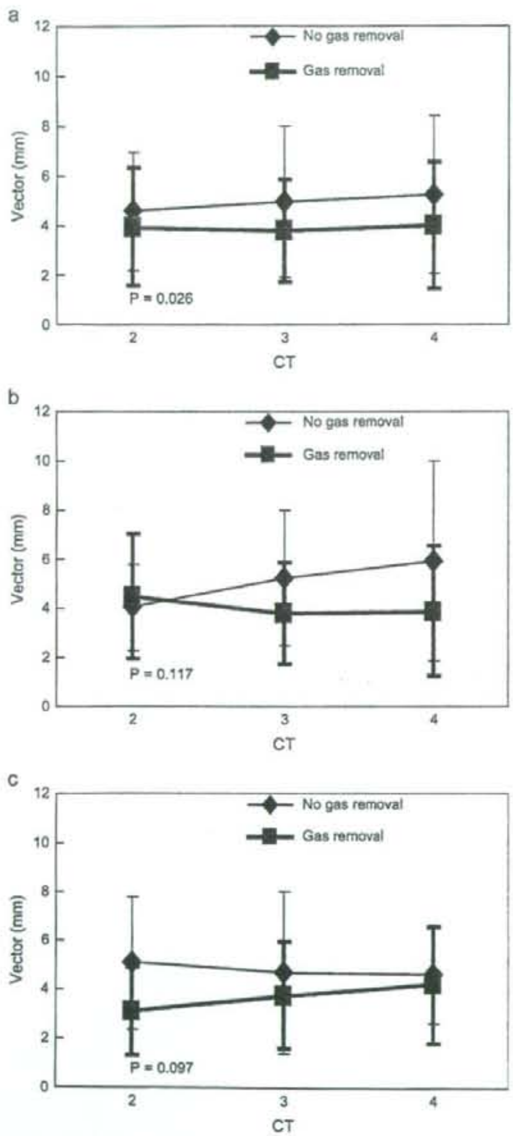

Fig. 4. Prostate vector (mean ± standard deviation) demonstrating center of mass displacement from initial treatment planning computed tomography. (a) All patients. (b) Non-whole pelvic radiotherapy arm. (c) Whole pelvis radiotherapy arm. CT = computed tomography.

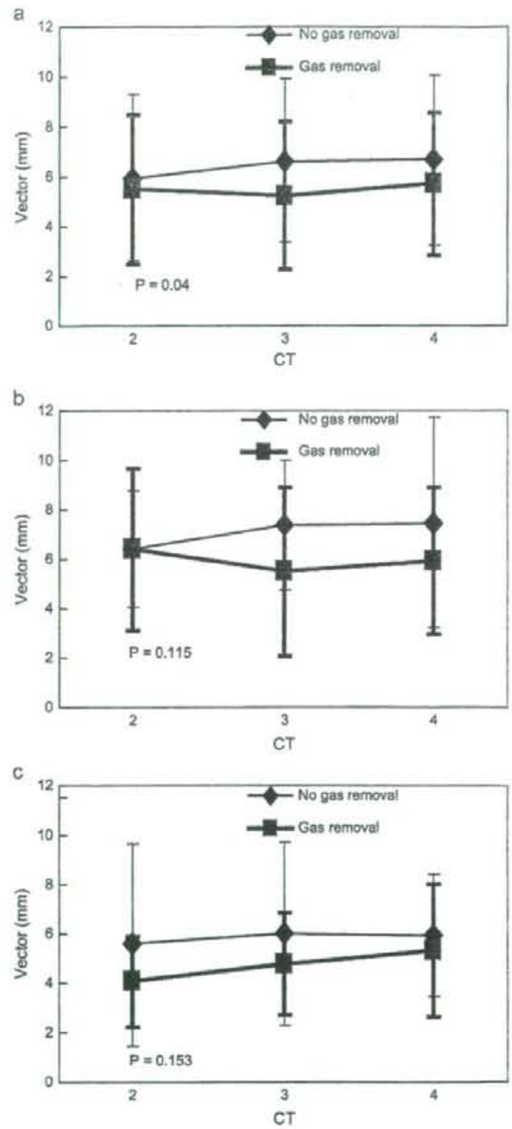

Fig. 5. Seminal vesicle vector (mean ± standard deviation) demonstrating center of mass displacement from initial treatment planning computed tomography scan. (a) All patients. (b) Non-whole pelvic radiotherapy arm. (c) Whole pelvis radiotherapy arm. CT = computed tomography.

CSA was <9 cm^2 in all 16 patients with gas removal in the WPRT arm. The mean ± SD and range of CSA in all patients and all CT scans before and during RT was 6.6 ± 2.2 cm^2 and 3.3–13.2 cm^2 without gas removal and 5.7 ± 1.9 cm^2 and 3.0–17.3 cm^2 with gas removal, respectively. The mean ± SD and range of CSA in the non-WPRT arm before and during RT was 6.6 ± 2.5 cm^2 and 3.3–13.2 cm^2 without gas removal and 5.8 ± 2.2 cm^2 and 3.0 to 17.3 cm^2 with gas removal, respectively. The mean ± SD and range of CSA in the WPRT arm was 6.6 ± 1.8 cm^2 and 3.8–13.2 cm^2 without gas removal and 5.4 ± 1.3 cm^2 and 3.2–8.8 cm^2 with gas removal, respectively.

The results of the prostate vector and seminal vesicle vector with or without gas removal are displayed in Figs. 4 and 5. No time trend was found by ANOVA. For prostate displacement, the vector with the rectal gas removal group was not significantly smaller in the non-WPRT arm ($p = 0.117$) or WPRT arm ($p = 0.097$), but was significantly smaller in all patients ($p = 0.026$) by ANOVA (Fig. 4). For seminal vesicle displacement, the vector for the rectal gas removal group was not significantly smaller in the non-WPRT arm ($p = 0.115$) or WPRT arm ($p = 0.153$), but was significantly smaller in all patients ($p = 0.04$) by ANOVA (Fig. 5). The vectors for the prostate and seminal vesicle displacement from the planning CT scan in all patients and all CT scans are shown in Table 1. The maximal, 90%, and 95% confidence limits of the prostate and seminal vesicle displacement vector in the rectal gas removal group were smaller than in the non–gas removal group (Table 1). The 95% confidence limit of the prostate displacement vector was reduced by 2.5 mm in all patients and 2.3 mm in the non-WPRT arm and 2.9 mm in the WPRT arm with rectal gas removal. The 95% confidence limit of the seminal vesicle displacement vector was reduced by 1.1 mm in all patients and 0.3 mm in the non-WPRT arm and 4.4 mm in the WPRT arm with rectal gas removal.

The motion distribution for the COM of the prostate and seminal vesicles from the planning CT scan for all patients and all scans in different groups (with and without rectal gas removal and in the non-WPRT and WPRT arms) is represented in Figs. 6 and 7, with its projection on two planes (Y and Z). The prostate motion occurred mainly along these two principal axes. The results depicted in Figs. 6 and 7 and the X direction are summarized in Tables 2 and 3. The mean displacements of the prostate and seminal vesicles were very close to 0 in the X, Y, and Z directions. The statistical significance of the overall SD for the COM of the prostate by rectal gas removal was noted in the X and Z directions ($p = 0.028$ and $p = 0.016$, respectively) in all patients and in the Z direction ($p = 0.047$) in the WPRT arm (Table 2). The 95% confidence limit displacements of the prostate COM (CLP) in the rectal gas removal group was smaller than in non–gas removal group in all directions. The 95% CLP was reduced by 0.8 mm in the X direction, 0.5 mm in the Y direction, and 2.8 mm in the Z direction for the non-WPRT arm with rectal gas removal. For the WPRT arm, the 95% CLP was reduced by 0.6 mm in the X direction, 3.5 mm in the Y direction, and 2.1 mm in the Z direction. In these groups, the overall SD and 90% and 95% CLP were smallest in the Y and Z directions for patients with rectal gas removal in the WPRT arm.

Statistical significance in the overall SD for the COM of the seminal vesicles by rectal gas removal was noted in the X ($p = 0.035$) and Z ($p = 0.002$) directions for all patients and in the X ($p = 0.035$) and Z ($p = 0.032$) directions for

Table 1. Vector for prostate and seminal vesicle displacement for all fractions and all patients

	Patients (n)	M (mm)	SD (mm)	*p*	Minimum (mm)	Maximum (mm)	90% CLV (mm)	95% CLV (mm)
Prostate								
All patients								
No gas removal	102	4.9	2.9	0.004	0.6	15.1	9.4	10.8
Gas removal	126	3.9	2.3		0.4	13.1	7.5	8.3
No WPRT								
No gas removal	48	5.1	3.1	0.041	1.2	15.1	10.4	10.8
Gas removal	78	4.1	2.4		0.4	13.1	8.1	8.5
WPRT								
No gas removal	54	4.8	2.7	0.023	0.6	12.3	8.5	10.4
Gas removal	48	3.7	2.1		0.6	9.1	6.7	7.5
Seminal vesicles								
All patients								
No gas removal	102	6.4	3.3	0.022	0.7	17.3	10.2	12.5
Gas removal	126	5.5	2.9		0.6	16.0	9.3	11.4
No WPRT								
No gas removal	48	7.1	3.1	0.05	1.9	17.3	11.4	12.4
Gas removal	78	5.9	3.2		0.6	16.0	11.2	12.1
WPRT								
No gas removal	54	5.8	3.4	0.05	0.7	16.8	10.2	13.5
Gas removal	48	4.7	2.2		1	11.2	7.7	9.1

Abbreviations: M = mean value for all fractions and all patients; SD = standard deviation for all fractions and all patients; CLV = confidence limit of vector; WPRT = whole pelvic radiotherapy.

p Values given for SD are results of *t* tests comparing deviations with and without gas removal.