Chapter 4

Great Role in Gynecological Cancer Prophylaxis of a Unique Health Check-Up Institute, Ningen Dock in Japan (Review)

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Abstract

In Japan, there are unique facilities (namely Ningen Dock) for health check-up that provide asymptomatic participants with a health examination, including cancer screening activities, at their own expense. The most advanced examination equipment and examinations do not only provide high accuracy, but they also reduce stress on the body of the client. Usage of the medical equipment and diagnostic techniques allows us for successful detection of many diseases in their early stages of development. This early detection leads to quicker response for the disease. On the other hand, gynecological cancer screening is a relatively simple, low cost, and noninvasive method. In this chapter, we introduce a major role of Ningen Dock in gynecological malignancy prophylaxis. Ningen Dock attendances are associated with extremely low positive gynecology cancer screening incidence (0.03%). The level of knowledge and attitude toward screening may be related to multiple factors such as ethnicity, place of residence, income, and social-economic status. Not paying attention to cancer screening may be the risk factors for non-attendance to health check-up. These findings are of importance for improving the gynecological cancer screening practices of the lower screening attendance in Japan.

Keywords: health check-up, Ningen Dock, gynecological cancer, attitude toward screening, cancer screening, cervical cancer

1. Introduction

Health and medical check-ups aim to discover problems that may be harmful to the future health of the examinees, providing proposals for health promotion support solutions. Health

check-ups focus on comprehensive assessments regarding the whole body even without disorders, while medical examinations include a specific disease or organ. In many countries, including Japan, a series of systemic routine health examinations and preventive medicine development in response to client needs undergo on a voluntary basis.

In Japan, there are unique facilities (namely Ningen Dock) for health check-up that provide asymptomatic participants with a health examination, including cancer screening activities, at their own expense [1]. Japan is indeed a country in the world with the most advanced medical devices. For example, about half of the CT scans and about one-third of the MRI scans are owned by medical facilities in Japan [2]. The most advanced examination equipment and examinations do not only provide high accuracy, but they also reduce stress on the body of the client. Usage of the medical equipment and diagnostic techniques allows us for successful detection of many diseases in their early stages of development. This early detection leads to quicker response for the disease.

The "OMOTENASHI" services provided by staffs, including nurses, technologists, and doctors, is supporting the popularity. With the careful client support underpinned by the Japanese culture of hospitality, the Ningen Dock in Japan is popular in neighboring countries. The number of people from another country is rapidly increasing, to visit Japan, to receive the medical services of Ningen Dock. These situations prompted us to introduce a major role of Ningen Dock in gynecological malignancy prophylaxis.

2. Gynecological examination flow

In general, there are three Ningen Dock programs, a half-day course, one-day course, and two-day course. Depending on the selection of the course, different diagnostic and procedural options are available. The cost is not covered by the social insurance. Asymptomatic women, aged from 18 until ~90 undergo medical evaluations, including a medical history, physical examination, blood sampling, urine sampling, and radiological imaging, as part of a routine health check-up and cancer screening (see **Table 1**). The popular plan for women is a gynecological cancer screening. Gynecologic examinations include uterine cytology (Papanicolaou test), transvaginal ultrasonography, and pelvic examination by a gynecologist.

Cervical and endometrial smears are performed using a speculum and/or brush. The cytology findings divided into seven groups: high-grade squamous intraepithelial lesions (HSIL), low-grade squamous intraepithelial lesions (LSIL), atypical squamous cells of undetermined significance (ASC-US), squamous cell carcinoma, atypical glandular cells (AGC), cervical adenocarcinoma, and normal. The cytological findings of endometrium are classified into four categories: suspected endometrial carcinoma, atypical endometrial cell, benign endometrial abnormality, and normal endometrium. When inadequate for classification, smears were again taken from examinees, and their smear samples are retrospectively reviewed if needed.

Abnormal cytologic and/or ultrasonographic findings introduce all examinees to the medical facilities for further managements. Even though no additional information are provided regarding their detailed examination outcomes, the present findings obtained from asymptomatic women may indicate annual gynecologic check-up and adequate follow-up programs

Basic examination (1-day course)	
Life Habits Check	Investigation of lifestyle through medical questionnaire, physical check-up, and advice on how to prevent the development of diseases and how to treat them.
Lungs	Chest X-ray to screening pulmonary disorders such as lung cancer, tuberculosis, and emphysema.
Heart	Screening for high blood pressure and cardiac disorder by electrocardiogram.
Digestive organs	Upper GI tests, abdominal ultrasonography, blood tests, and stool analysis to screen gastrointestinal diseases such as cancer, ulcer, polyp, and dysfunction of liver and pancreas by investigating esophagus, stomach, duodenum, liver, pancreas, and gallbladder.
Eyes	Screening for cataract, glaucoma, and visual change by fundus photography and intraocular pressure measurement.
Breast	X-ray and ultrasonography
Gynecology	Screening for gynecological disorders such as uterine cancer and ovarian tumors through pelvic examination, cervical cytology and ultrasonography. Tumor markers (CA125, CA72-4, CA19-1, and SCC) are optional.
Others	Screening tests for hearing, infections such as hepatitis virus and syphilis and determining blood type.
Optional	
This course is arranged for those who want to take an opportunity to refresh and receive the screening in a more relaxed manner. The courses contain optional examinations that can be added upon the request.	

Table 1. Test items of Ningen dock.

against symptom-free population, and this can cause remarkable reduction in the probability of malignant disease. The study sample is derived from the representative population of high-income and high-attitude toward health maintenance, providing most of our observations as important implications in terms of public health.

If anything abnormal is found, the participants are provided the most appropriate advice, by determining whether follow-up observations would be sufficient, or if medical treatment is required, what kind of medical treatment should be provided, and what facility would be appropriate for a particular treatment.

3. Incidence of positive gynecological cancers in examinees of Ningen Dock

Table 2 shows the cytologic and ultrasonographic findings of all subjects who visited the Ningen Dock in our institute between 2002 and 2016 [3, 4]. Of the cytology from cervix, 140 cases (0.8%)

were found as abnormal. Among them, 127 cases were classified as low-grade cervical smear abnormalities: LSIL and HSIL were seen in 105 cases, ASC-US was seen in 22. Suspected malignancy of squamous cell was detected in five cases within this study period, while case of cervical adenocarcinoma was not found. No cytological abnormality categories were clustered in any specific age group. Endometrial smear showed hyperplasia suspicious in 2.7% cases.

Uterine enlargement was the most frequently detected gynecologic finding, with a peak reaching approximately 25% in 40–49 years age group. The uterine abnormalities had a tendency to decrease in those aged over 60 years. Ovarian tumor (including solid and cystic enlargement) was detected in 5.2–8.0% of those in the age groups of 30–49 years, while those aged over 60 years had less frequency. In 91.3% participants, no gynecologic abnormality was detected.

The abnormal cytologic findings, including dysplastic changes and cervical cancer, are observed to be very low compared with other studies performed in developed countries (3.4–9%) [5–10]. Our findings based on 2011–2016 Ningen Dock records are similar to those of the former observations, and most of participants (95.6%) revealed no gynecological cytology

Age group (years)	No. (%)	Cytology					Uterine tumor and abnormalities	Ovary tumor and abnormalities	Others*
		Cervix				EM			
		LSIL	HSIL	ASC-US	SCC	Other than normal			
<19	12 (<0.1)	1 (<0.1)	0	0	0	0	0	2 (0.1)	0
20–29	794 (4.8)	9 (0.6)	0	5 (0.3)	1 (<0.1)	0	6 (0.4)	18 (1.3)	13 (0.9)
30–39	3172 (19.2)	26 (1.8)	4 (0.3)	3 (0.2)	0	1 (<0.1)	80 (5.6)	74 (5.2)	68 (4.7)
40–49	6217 (37.6)	37 (2.6)	6 (0.4)	3 (0.2)	1 (<0.1)	2 (0.1)	361 (25.2)	114 (8.0)	139 (9.7)
50–59	4615 (27.9)	22 (1.5)	4 (0.3)	9 (0.6)	2 (0.1)	35 (2.4)	164 (11.4)	42 (2.9)	95 (6.6)
60–69	1464 (8.9)	4 (0.3)	0	2 (0.1)	1 (<0.1)	0	44 (30.7)	8 (0.6)	16 (1.1)
70–79	228 (1.4)	0	0	0	0	0	5 (0.3)	1 (<0.1)	6 (0.4)
> 80	18 (<0.1)	0	0	0	0	0	0	0	0
Total	16,520 (100)	99 (0.6)	14 (<0.1)	22 (0.1)	5 (<0.1)	37 (0.2)	660 (4.0)	259 (1.6)	337 (2.0)
						1433 (8.7)			

Between January 2002 and December 2016, 16,520 asymptomatic women, aged 18–85, visited the Ningen Dock in Matsunami General Hospital for their gynecological health check-up. *Including vaginosis, leukoplakie, Bartholin cyst, posthysterectomy, cervical polyp, and prolaps/ptosis. LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; ASC-US, atypical squamous cells of undetermined significance; SCC, cervical squamous cell carcinoma; AGC, atypical glandular cells; EM; endometrium. Modified from our previous reports [3, 4].

Table 2. Gynecologic findings of participants distributed by age group.

and ultrasonographic abnormalities. Gynecologic cancer is detected in 0.03%, all of which were at the early stages (so-called CIN3). The very low incident is in good agreement with the primary report in some Ningen Docks [1, 11].

HPV stands for human papilloma virus, which is a group of more than 200 viruses. Most people will get a HPV infection during their lifetime, usually from sexual activity. Most of these infections do not need treatment, but they can cause genital warts. In some, however, HPV infection causes changes in the cervix that can develop into cervical cancer. HPV can infect the cells on the surface of the cervix and damage them, causing their appearance to change and lead to abnormalities in these cells over a number of years. These abnormalities are known as cervical intraepithelial neoplasia (CIN). These changes are classified according to their severity. The mean time between the virus infection and invasive cancer takes about 15 years, and within 2–4 years of detection 15.5–25.5% of low-grade epithelial lesions that become high-grade lesions. In some cases, these more severe changes can develop into cervical cancer. The progression of mild and severe changes to cancer takes many years so these abnormalities are known as precancerous [12–14]. HPV infection is most common in people in their late teens and early 20s [15, 16]. A study in Jordan, one of the most conservative and religious country, found that 0.8% of 1176 women aged 18–70 years are classified as ASC-US and 0.2% as LSIL. In our unique system Ningen Dock in Japan, symptom-free women undergo medical check-up at their own expense. Their educational tradition and high concern on sex-transmitted infection, such as HPV, may restrict the likelihood of multiple sexual partners. This may be the most plausible explanation for extremely low incidence of dysplastic changes and cervical cancer found in our study group of women.

As uterine enlargement, uterine myoma with or without adenomyosis are found in 20–25% of reproductive-age women, indicating that they are one of the most frequent women's lower abdominal tumor [17–19]. The women with myoma do not necessarily complain of symptoms, and even large ones may go undetected by the patient, particularly if she is obese. Myoma-linked symptoms (abdominal distention, vaginal bleeding, constipation, and peritoneal irritation) depend on their location, size, and state of presentation; symptoms are present in 35–50% of patients with myomas. Ovarian tumors, cystic or solid, also seldom cause symptoms. Although the ovarian enlargement is frequently undetected by the patients, the diagnosis of these tumors is not usually difficult by ultrasonographic examination at physical check-up. Our subjects showed lower frequency of uterine enlargement and ovarian tumors.

Many previous trials demonstrated a reduction in the average overall mortality among ovarian cancer patients screened with an annual sequential, multimodal strategy that tracked biomarkers CA125 over time, where increasing serum CA125 levels prompted ultrasound [20–23]. A critical factor which could contribute to false negatives is that many aggressive ovarian cancers are believed to arise from epithelial cells on the fimbriae of the fallopian tube, which are not readily imaged. In addition, because, only a fraction of metastatic tumors may reach an imaging device-detectable size before they metastasize, annual screening with imaging diagnosis may fail to detect a large fraction of early stage ovarian cancers [24, 25]. The ability to detect ovarian carcinomas before they metastasize is critical and future efforts toward improving screening should focus on identifying unique features specific to aggressive, early

stage tumors, as well as improving imaging sensitivity to allow for detection of tubal lesions. So far, multimodal screening strategy in which blood-based assay is positive, and subsequent imaging examination may prove useful in detecting early stage cases [20–22, 25].

4. Gynecological cancer screening intervals

In many countries, undergoing cancer screening is not mandatory but voluntary. Many women are advised to annual gynecological screening for more than a decade. Recently, recommendations of many developed countries include one Pap smear every 3 years after two annual negative results from the age of 18 until 69 years [26]. According to the current American Cancer Society guidelines, adequate negative prior screening and no history of CIN 2 of higher recommend that cervical smear test stops at age 65 [27]. On the other hand, annual screening continues among women of 65 years of age and older, even among those with less than a 5-year life expectancy due to poor health [28]. Likely, as clinical practice continues to change around the screening pelvic examination, consequent changes in utilization of reproductive health services among young adolescence to postmenopausal.

First care visit volume is a key step for continuous use of an extended screening interval, with women who report to first gynecologic care visit during the last year being over 10 times more likely to report current use of a 3-year screening interval than those with three or more visits. It is not possible to separate which come first of less-frequent care seeking and an extended gynecological cancers (including uterine and ovarian malignancies) screening interval. Clearly, some women are screened on 3-year intervals by default; however, others who purposefully follow an extended screening interval may have no perceived need to seek care during a given year.

The continuous screening preference of Japanese women may reflect long-held beliefs about the importance of annual cervical smear examinations and pelvic ultrasonographic examination with limited awareness of the potential harms associated with this practice. The level of knowledge and attitude toward screening are related to multiple factors such as ethnicity, place of residence, income, and social-economic status [29]. From an examiner perspective, annual gynecologic cancer screening has facilitated regular contact with examinees. In general, women are invited by their gynecologists for the examination. The cytologic screening time interval depends on the doctor's personal judgment [30]. If he feels that the test will benefit their patients, the likelihood of performing the test increases. Some systemic review found a positive correlation of educational level, financial status, and an awareness of the mortality rates associated gynecological cancer with gynecological cancer attendance [26, 31, 32]. The level of knowledge and attitude toward health check-up are related to multiple factors such as ethnicity, place of residence, income, and social-economic status [33–37].

5. Discussion

Uterine cancer, in particular cervical cancer, is preventable. More than half of the women diagnosed with cervical cancer have not attended screening in the past 3 years. A community-based screening strategy is one of the greatest success stories in cancer prevention, and widespread

screening reduces the cervical cancer incidence worldwide [38–42]. The mean time between the virus infection and invasive cancer takes about 15 years, and within 2–4 years of detection 15.5–25.5% of low-grade epithelial lesions become high-grade lesions. In some cases, these more severe changes can develop into cervical cancer [5–10]. A routine screening test includes cytology smear test used for the detection of early cervical abnormalities (precancerous dysplastic changes) of the uterine cervix [5–10]. The screening is a relatively simple, low cost, and noninvasive method. Concurrent transvaginal ultrasonography for detection of ovarian and uterine tumors, the cervical and endometrial cytology smear tests attenuate the probability of developing gynecological malignant diseases.

Ningen Dock check-ups provide an occasion to realize preventive medicine. An important aim of gynecological health check-up is to provide support in improving the risk factors that accelerate the risk of outbreak of a malignant disease at an early stage, before subjective symptoms become apparent. Additionally, meticulous educational guidance is provided to match individual living patterns, education level, and ways of thinking. Ningen Dock can also conceive of time in the future when more appropriate and effective educational advice could be continuously provided according to a participant cultural background and lifestyle habits, via collaboration with health-related public services.

Qualitative evaluation of Ningen Dock Facilities consists of documentation and an inspection. These are administration of the facility, satisfaction and safety of examinees, and quality of check-up and follow-up [1]. Recently, the usefulness of Ningen Dock has greatly increased not only in the primary, but also in the secondary prevention of non-communicable diseases due to advances in diagnostic medical technology and therapeutic medicine. However, one of the problems is that relatively large numbers of Ningen Dock examinees who require a second, more detailed examination do not have the examination that has been recommended. For instance, only 61% of the Ningen Dock examinees who required total colon fiberscope as a second, detailed examination due to a positive fecal occult blood test underwent it. Similar tendencies were recognized for almost all Ningen Dock examinations [11]. The reason why Ningen Dock examinees who need second, more detailed examinations do not have them may be that most of them do not understand the importance of such examinations for the early detection of non-communicable diseases and their risk factors because we do not adequately explain the need for more detailed examinations to examinees. Therefore, better education of examinees may be urgently needed in order to further increase the usefulness of Ningen Dock.

In Japan, there are also free physical check-up programs of cancer screening, by which asymptomatic participants undergo a medical examination at public expense. Takagi et al. [43] reported similar data using records of the public expense-covered free examination, and suggested that active gynecologic check-up and adequate follow-up programs even against symptom-free population can reduce in the probability of malignant disease development. Their findings from representative population of high-attitude toward screening, but non-high income, may give new insight into the terms of public health.

The present data are from subject to the limitations of any analysis of self-covered health check-up survey data from participants of Ningen Dock in Japan. Although data are weighted to reflect the Japanese population, the extent to which results are generalizable is no known. Future studies, extended to non-Asian, should attempt to oversample racial minorities and include a detailed assessment of gynecologic cancer screening history and follow-up treatment.

Women attitudes and beliefs related to screening frequency may differ if they reflected truly informed preference and may be related to less screening. The present chapter introduced the extremely low positive gynecology cancer screening incidence in Ningen Dock participants, providing the active strategy in the gynecological cancer screening practices of the lower screening attendance in Japan. However, strategies may be needed to encourage examiners to adopt recommended screening intervals and to educate women about the reasoning behind less-than-annual testing, including explicit discussions about the meaningless and potential harms associated with excess screening.

Disclosure statement

The authors declare no conflict of interest.

Author's contribution

AI designed the study and drafted the manuscript. AI managed all data and performed the analyses. All authors participated in the gynecological examinations at Ningen Dock and commented on various drafts and approved the final version of the manuscript.

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