Chapter 4■Post-treatment Follow-up

Overview

In Japan, routine follow-up after treatment for uterine body cancer includes a combination of pelvic examination, vaginal cytology, transvaginal ultrasonography, tumor marker measurements, plain chest radiography, and CT scanning. In Western countries, the rate of diagnosis of recurrent disease was higher when patients presented to hospitals of their own judgment with symptoms than at routine follow-up. The literature increasingly contains reports that question the necessity of routine follow-up, also from the economic viewpoint. There is a trend to recommending longer intervals between follow-up appointments, and even discontinuing routine follow-up due to the lack of evidence of clinical benefit. In Western countries, standard postoperative follow-up often does not include tumor markers and diagnostic imaging such as CT scanning due to their cost. Since diagnosis of recurrence is made in only a small number of patients by vaginal cytology alone and its high cost, there is a tendency to eliminate it from routine follow-up in Western countries. However, even in Western countries many are of the opinion that the following are necessary in patients at high risk of recurrence: pelvic examination, vaginal cytology, and in some cases CA125 measurements. The goal of routine follow-up is the early detection of recurrence, although it is unclear whether follow-up improves the survival rate. In the future, routine follow-up needs to be reevaluated in Japan. It will probably be advisable to individualize follow-up for each patient.

CQ24

What intervals are recommended for post-treatment follow-up?

Recommendations

Intervals between routine follow-up appointments are as shown below (Grade E):
Every 1-3 months for the first 1-3 years after treatment
Every 6 months for the 4th and 5th years after treatment
Annually from the 6th year after treatment

Background and Objectives

In Western countries, a typical follow-up protocol after uterine body cancer is every 3-4 months for 1-2 years after treatment and every 6 months to 1 year thereafter. The rate of diagnosis with recurrence is higher for patients when they present to hospital by their own judgment because of symptoms than at routine follow-up. The literature increasingly contains reports that question the necessity of routine follow-up, also from the economic viewpoint.[1-5] There is a trend to recommending longer intervals between follow-up appointments, and even discontinuing routine follow-up due to the lack of evidence of clinical benefit. In Japan, many institutions perform routine follow-up at intervals of 1-3 months for 1-3 years after uterine body cancer treatment. We examined recommended follow-up intervals after uterine body cancer treatment.

Explanations

In Western countries, the literature increasingly contains studies recommending longer intervals between routine follow-up appointments.[1-5] For example, Shumsky et al. reviewed 317 subjects in a follow-up study of follow-up after uterine body cancer treatment, in which subjects attended routine follow-up every 3 months for the first year after treatment, every 4 months for the second year, and every 6 months thereafter. Follow-up included pelvic examination, vaginal cytology, and biannual plain chest radiography. Recurrence was diagnosed at routine follow-up in 11 subjects (21% of subjects with recurrence), and in 42 subjects (79%) because symptomatic patients presented to hospitals by their own judgment. Vaginal cytology was not diagnostic in any subjects. No significant difference was seen in survival rates after recurrence between the group diagnosed at routine follow-up and the group diagnosed after presenting with symptoms. They concluded that routine follow-up did not improve early diagnosis of recurrence or survival rates.[2] Similarly, Owen et al. reviewed 102 subjects in a study of follow-up after uterine body cancer treatment. They investigated mainly the interval until recurrence and interval from recurrence until death. No significant differences were seen in outcomes or the interval until recurrence between the group diagnosed with recurrence at routine follow-up and the group diagnosed after presenting with symptoms. They found that routine follow-up is not clinically useful.[3] Early detection of recurrence at routine follow-up does not necessarily result in improved outcomes.

Differences exist between Japan and Western countries in follow-up protocols and medical systems. There is accordingly insufficient evidence to make any urgent recommendations for markedly longer intervals between appointments, or elimination altogether of routine follow-up. Some opinions expressed in the Western literature recommend follow-up in high risk patients including pelvic examination, vaginal cytology, and in some cases CA125 measurement.[1,2,5] In Japan, 90% of recurrences are reported to occur within 2 years.[6,7] In Western countries, at least 75% of recurrences are reported to occur within 3 years.[1-5,8-11] Some Japanese institutions perform follow-up at relatively short intervals of 1-2 months for the first 1-3 years after treatment.[7] In the Western literature, approximately 20% of G1 uterine body cancer recurrences occurred ≥5 years after initial treatment. Follow-up is therefore recommended for ≥5 years after treatment.[6,7]

The risk of recurrence depends mainly on stage, histology, and completeness of surgery. The risk of recurrence should be considered on an individual basis, and follow-up planned accordingly. If large-scale clinical trials are performed in Japan, it may be possible to recommend greatly increased follow-up intervals, as is becoming the practice in Western countries.

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CQ25

Is measuring serum CA125 and CA19-9 useful in post-treatment follow-up?

Recommendations

The merits of measuring CA125 and CA19-9 have not been established (Grade C).

Background and Objectives

We examined the usefulness of measuring serum CA125 and CA19-9 in follow-up after initial treatment.

Explanations

For uterine body cancer, reported CA125 positive rates by surgical stage were 10.0-21.0% for stage I, 14.3-60.8% for stage II, 0-75.0% for stage III, and 66.7-91.0% for stage IV.[1-6] Reported CA19-9 positive rates were 15.0-29.7% for stage I, 11.1-32.0% for stage II, 0-55.9% for stage III, and 27.0-54.5% for stage IV.[1-6] The reported CA125 positive rate for recurrent cases is 41.6-65.6%.[1-6] One study stated that the risk of recurrence can be stratified according to preoperative CA125 levels.[5] Another report stated that 62.9% of recurrent cases showed elevated tumor marker levels at an average 2.4 months prior to the confirmation of recurrence by radiological, cytological or histological diagnosis.[6] Determination of CA125 and CA19-9 levels may be clinically important in the early detection of metastases and recurrences after treatment. Other combination assays besides CA125 and CA19-9 have included carcinoembryonic antigen (CEA), CA15-3, CA72-4, and CA602.[1-6]

According to the Western literature, tumor markers are not routinely included in postoperative follow-up protocols.[7-10] The frequency of detection of recurrence was 26% in asymptomatic recurrent cases using CA125, but some are of the opinion that it should only be measured in selected patients due to its cost.[11]

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CQ26

Are pelvic examination and vaginal vault smears useful in post-treatment follow-up?

Recommendations

(1) Since pelvic recurrences account for 30-65% of recurrences, pelvic examination is useful (Grade A').
(2) Vaginal vault smears should be part of routine post-treatment follow-up (Grade E).

Background and Objectives

We examined the usefulness of pelvic examination and cytology as part of postoperative follow-up.

Explanations

According to the literature, 30-60% of the recurrences are intrapelvic,[1-10] and pelvic examinations are useful. Few recurrences are diagnosed by cytology alone, and its cost is high, so cytology tends not to be included in standard follow-up in the U.S. and Europe.[6,7,11,12] The rate of diagnosis of recurrence is reportedly higher when patients present to hospital with symptoms than at routine follow-up. Routine follow-up itself has been considered to be of no clinical or economic benefit and some have recommended its discontinuation.[6,12] In some cases, however, cytology can be useful in the early diagnosis of recurrence in the vaginal stump,[4] and there is not enough evidence to recommend the immediate elimination of vaginal vault smears from routine follow-up.

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CQ27

Are plain chest radiography and other diagnostic imaging methods useful in post-treatment follow-up?

Recommendations

(1) Plain chest radiography performed annually or biannually is useful for the early detection of recurrences (Grade C).
(2) Diagnostic imaging should be performed annually or biannually (Grade E).

Background and Objectives

We examined the usefulness of plain chest radiography and other diagnostic imaging methods as part of post-operative follow-up.

Explanations

Uterine body cancer has a high frequency of distant metastasis to the lungs. The benefits of plain chest radiography are uncertain as part of postoperative follow-up. According to the literature, the lung is the site of recurrence in 5-23% of patients.[1-4] Autopsy findings identify metastases was the lung in 41% of cases, indicating that it is the most frequent site, followed by the peritoneum (39%), ovary (34%), liver (29%), and the gastrointestinal tract (29%).[5] Plain chest radiography is therefore considered useful in screening for recurrence. However, lung metastases are detected on plain chest radiographs in 0-55% of asymptomatic patients. Studies vary in their conclusions as to whether to include plain chest radiography in routine follow-up, and how often.[2,6-8]

The literature from Western countries indicates that the following diagnostic imaging methods are not included in routine follow-up due to their cost: CT, MRI, and PET scanning, and Ga and bone scintigraphy.[1-3,6-8] Although PET scanning is not used in screening for the early detection of recurrences, it is useful when recurrence is clinically suspected.[9-11] Since CT scanning allows imaging of a relatively wide area in a short period of time, it is useful in the detection of metastases, including to the pelvic and para-aortic lymph nodes, and looking for recurrences.[12] However, no improvement in outcomes resulted from CT detection of recurrence.[13] There is also the issue of radiation exposure, and the indications for diagnostic imaging need to be considered carefully.

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