US Preventive Services Task Force | Recommendation Statement

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Screening for Pancreatic Cancer
US Preventive Services Task Force Reaffirmation Recommendation Statement

US Preventive Services Task Force

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Abstract

Importance Pancreatic cancer is an uncommon cancer with an age-adjusted annual incidence of 12.9 cases per 100 000 person-years. However, the death rate is 11.0 deaths per 100 000 person-years because the prognosis of pancreatic cancer is poor. Although its incidence is low, pancreatic cancer is the third most common cause of cancer death in the United States. Because of the increasing incidence of pancreatic cancer, along with improvements in early detection and treatment of other types of cancer, it is estimated that pancreatic cancer may soon become the second-leading cause of cancer death in the United States.

Objective To update the 2004 US Preventive Services Task Force (USPSTF) recommendation on screening for pancreatic cancer.

Evidence Review The USPSTF reviewed the evidence on the benefits and harms of screening for pancreatic cancer, the diagnostic accuracy of screening tests for pancreatic cancer, and the benefits and harms of treatment of screen-detected or asymptomatic pancreatic cancer.

Findings The USPSTF found no evidence that screening for pancreatic cancer or treatment of screen-detected pancreatic cancer improves disease-specific morbidity or mortality, or all-cause mortality. The USPSTF found adequate evidence that the magnitude of the benefits of screening for pancreatic cancer in asymptomatic adults can be bounded as no greater than small. The USPSTF found adequate evidence that the magnitude of the harms of screening for pancreatic cancer and treatment of screen-detected pancreatic cancer can be bounded as at least moderate. The USPSTF reaffirms its previous conclusion that the potential benefits of screening for pancreatic

Conclusions and Recommendation The USPSTF recommends against screening for pancreatic cancer in asymptomatic adults. (D recommendation)

Introduction

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendation and Evidence

The USPSTF recommends against screening for pancreatic cancer in asymptomatic adults (D recommendation) (**Figure 1**).

Figure 1. USPSTF Grades and Levels of Evidence

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USPSTF indicates US Preventive Services Task Force.

Rationale

Importance

Pancreatic ductal adenocarcinoma (referred to hereafter as pancreatic cancer) is an uncommon cancer with an age-adjusted annual incidence of 12.9 cases per 100 000 person-years. However, the death rate is 11.0 deaths per 100 000 person-years because the prognosis of pancreatic cancer is poor.[1] Although its incidence is low, pancreatic cancer is the third most common cause of cancer death in the United States. Based on data from the Surveillance, Epidemiology, and End Results Program from 2009 to 2015, the overall 5-year survival rate for pancreatic cancer is 9.3%, and survival rates vary depending on the stage at which it is diagnosed. The 5-year survival rate for localized pancreatic cancer is 37.4%; when regional disease is present, the 5-year survival rate is 12.4%, and when distant metastatic disease is present, the 5-year survival rate is 2.9%.[1] Surgical intervention at an early stage is the treatment most likely to improve chances of survival; however, most cases of pancreatic cancer are detected at an advanced stage,[1] when surgical resection is not likely to be beneficial. Because of the increasing

it is estimated that pancreatic cancer may soon become the second-leading cause of cancer death in the United States.[2]

In 2019, an estimated 56 770 persons will be diagnosed with pancreatic cancer and 45 750 persons will die of the disease.[1] About 85% to 90% of persons diagnosed with pancreatic cancer do not have known familial risk or genetic syndromes, 5% to 10% of persons have familial risk, and 3% to 5% of cases are due to inherited genetic cancer syndromes (such as Peutz-Jeghers syndrome). Familial pancreatic cancer is defined as a kindred with at least 2 affected first-degree relatives; a person's degree of familial risk depends on the number of affected relatives.[3-5]

Reaffirmation Process

In 2004, the USPSTF reviewed the evidence on screening for pancreatic cancer in asymptomatic adults and issued a D recommendation. The USPSTF decided to use a reaffirmation deliberation process to update this recommendation. The USPSTF uses the reaffirmation process for existing A or D grade recommendations for which only a very high level of evidence would justify a change in the grade of the recommendation. In its deliberation of the evidence, the USPSTF considers whether the new evidence is of sufficient strength and quality to change its previous conclusions about the evidence.

Detection

The USPSTF found no evidence on the accuracy of imaging-based screening tests (computed tomography [CT] scan, magnetic resonance imaging [MRI], or endoscopic ultrasonography [EUS]) for detecting pancreatic cancer.

Benefits of Detection and Early Treatment

The USPSTF found no evidence that screening for pancreatic cancer or treatment of screen-detected pancreatic cancer improves disease-specific morbidity or mortality, or all-cause mortality. Based on the low incidence of pancreatic cancer in the general population, the uncertain accuracy of current candidate screening tests, and the poor prognosis for pancreatic cancer even when treated at an early stage, the USPSTF found adequate evidence to bound the benefits of screening for pancreatic cancer in asymptomatic adults as no greater than small. When direct evidence is limited, absent, or restricted to select populations or clinical scenarios, the USPSTF may place conceptual upper or lower bounds on the magnitude of benefit or harms.

Harms of Detection and Early Treatment

The USPSTF found adequate indirect evidence to bound the magnitude of the harms of screening for pancreatic cancer and treatment of screen-detected pancreatic cancer as at least moderate, based on potential harms from false-positive results and the harms of treatment.

USPSTF Assessment

Using a reaffirmation deliberation process, the USPSTF concludes that there is no new evidence that warrants a change in the prior D recommendation and reaffirms its previous conclusion that the potential benefits of screening for pancreatic cancer in asymptomatic adults do not outweigh the potential harms.

Clinical Considerations

This recommendation applies to asymptomatic adults not known to be at high risk of pancreatic cancer (**Figure 2**). Therefore, this recommendation does not apply to persons at high risk of pancreatic cancer due to an inherited genetic syndrome (eg, Peutz-Jeghers syndrome, hereditary pancreatitis) or due to a history of familial pancreatic cancer.

Figure 2. Clinical Summary: Screening for Pancreatic Cancer

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Assessment of Risk

Persons with certain inherited genetic syndromes or a history of familial pancreatic cancer are at high risk of pancreatic cancer. This recommendation does not apply to these high-risk populations.

Other factors such as new-onset diabetes, preexisting diabetes, older age, cigarette smoking, obesity, or a history of chronic pancreatitis increase risk to a lesser degree. The USPSTF considers asymptomatic persons who have these other risk factors part of the general population, and they are included in this recommendation.

Screening Tests

The USPSTF does not recommend screening for pancreatic cancer in the general population using any method. Imaging-based methods, such as the CT scan, MRI, and EUS, have been studied as screening tests in trials of screening persons at high risk of pancreatic cancer due to inherited genetic syndromes or familial pancreatic cancer. There currently are no accurate, validated biomarkers for early detection of pancreatic cancer.[6-11]

Treatment or Interventions

Surgery (pancreaticoduodenectomy [known as the Whipple procedure] or total or distal pancreatectomy) is the generally recommended treatment for pancreatic cancer deemed to be resectable at the time of diagnosis. Neoadjuvant or adjuvant chemotherapy may be recommended, depending on the stage of cancer and other factors.

Other Considerations

Research Needs and Gaps

Research is needed to develop effective screening tests with high sensitivity and high specificity for pancreatic cancer and, ideally, high-grade precursor lesions. Research is needed to better understand the prevalence and natural history of precursor lesions to pancreatic cancer, including the likelihood of progression of precursor lesions to pancreatic cancer.

Studies investigating the benefits and harms of screening for pancreatic cancer in persons at high risk because of a

improved clinical outcomes) and harms of screening for pancreatic cancer in this population. If a net benefit of screening is found in high-risk persons, studies of screening in persons who may be at increased risk (eg, adults with new-onset diabetes) may be warranted. Research on improved risk stratification may also help advance the field of pancreatic cancer screening.

In addition, pancreatectomy carries a significant risk of morbidity and mortality, and the prognosis for more advanced pancreatic cancer, which is not amenable to surgery, is poor. Research on better treatments for all stages of pancreatic cancer to improve long-term survival and decrease the harms of treatment is needed.

Discussion

Burden of Disease

Pancreatic cancer is uncommon, with an estimated incidence of 12.9 cases per 100 000 person-years. It has a poor prognosis, with an overall 5-year survival rate of 9.3%.[1] Surgical intervention at an early stage is the treatment most likely to improve chances of survival; however, most cases of pancreatic cancer are detected at an advanced stage,[1] when surgery is not likely to improve the survival rate. In 2019, an estimated 56 770 persons will be diagnosed with pancreatic cancer, and 45 750 persons will die of it, making it the third most common cause of cancer death in the United States.[1]

Scope of Review

To update its 2004 recommendation on screening for pancreatic cancer, the USPSTF commissioned a systematic review on the benefits and harms of screening for pancreatic cancer, the diagnostic accuracy of screening tests for pancreatic cancer, and the benefits and harms of treatment of screen-detected or asymptomatic pancreatic cancer.[12,13] The USPSTF considered studies of screening in persons at high risk of pancreatic cancer due to familial history to determine whether this evidence might help inform its recommendation on screening for pancreatic cancer in the general population.

Accuracy of Screening Tests

The USPSTF found no studies that reported on the sensitivity or specificity of CT scan, MRI, or EUS as screening tests for pancreatic cancer.

The USPSTF found 13 cohort studies of screening for pancreatic cancer, mostly in persons at high familial risk, using CT scan, MRI, or EUS (n=1317) that reported on the yield of screening.[14-26] One study also included screening in a group of 161 participants who did not have known familial or genetic risks and detected no cases of pancreatic cancer in this group.[22] Among high-risk participants in all studies, a total of 18 cases of pancreatic cancer were found across all rounds of screening, for a yield of 15.6 cases per 1000 persons.[12,13] The applicability of these data to persons not at high risk of pancreatic cancer is uncertain, and the yield of screening in a population with a lower incidence of pancreatic cancer is likely to be much lower. Another important consideration is that any screening test used in a population with a lower incidence of pancreatic cancer would potentially have a lower positive predictive value and a higher rate of false-positive results.

Effectiveness of Early Detection and Treatment

The USPSTF found no studies on the benefits of screening for pancreatic cancer or on the benefits of treatment of

In the 13 cohort studies of screening in persons at high familial risk, a total of 57 screened patients underwent pancreatic surgery. Of the 57 patients undergoing surgery, 14 were found to have pancreatic cancer, 38 had precursor lesions (intraductal papillary mucinous neoplasm, pancreatic intraepithelial neoplasia, or both), and 5 had neuroendocrine tumors, liver hyperplasia, or a benign serous cystadenoma.[12] Because the risk of progression of precursor lesions (particularly low-grade lesions) to invasive cancer is not clear, the balance of the potential benefits or harms of detecting and undergoing pancreatic surgery to remove such lesions is unknown. Pancreatic intraepithelial neoplasia is common, and most cases do not progress to cancer. In 2 studies, 26% to 54% of pancreata removed at surgery for reasons other than pancreatic cancer contained such lesions.[27,28] Another retrospective study, describing the experience at 3 US cancer centers with surgical resection of intraductal papillary mucinous neoplasms,[29] found that the International Consensus Guidelines criteria for the management of intraductal papillary mucinous neoplasms of the pancreas[30] had high sensitivity (98.4%) but low specificity (14.8%) to predict high-grade dysplasia or invasive cancer. These data suggest the possibility that screening in the general population might lead to overdiagnosis and overtreatment.

In the screening studies of high-risk persons, a total of 18 cases of pancreatic cancer were detected. As noted above, 14 of these cases were confirmed by surgery. The remaining 4 cases were detected with advanced-stage nonresectable disease. Twelve of the cases (66.7%) were detected at stage I or II or were classified as "resectable."[12,13] Of the 18 detected cases of pancreatic cancer, longer-term follow-up was reported for only 10. Among those 10 cases, 5 persons were alive at 12 to 63 months of follow-up, 2 of whom were reported to have distant metastases.[12] These data are limited by incomplete reporting of follow-up for detected cases and by the small number of cases. The USPSTF did not find studies that compared health outcomes for screened and unscreened populations to determine the effectiveness of screening. In addition, the applicability of these results to a population not at high risk is uncertain.

Potential Harms of Early Detection and Treatment

The USPSTF reviewed 10 cohort studies of screening for pancreatic cancer in high-risk persons to assess the potential harms of screening and treatment. In 2 studies (n = 271) that assessed the psychosocial harms of screening, the majority of participants reported normal levels of distress or worry at all time points.[31,32] One study reported no change in levels of perceived pancreatic cancer risk, worry, and general distress at baseline and 3 months after screening,[31] while a second study reported Cancer Worry Scale scores that decreased over time (compared with baseline scores).[32]

Eight studies reported on procedure-related harms of screening.[14,15,17-22] In 1 study of 216 persons who underwent EUS, 55 (25.5%) reported mild postprocedure pain, and 13 (6.0%) reported adverse events related to anesthesia.[22] Of 150 persons in 2 studies who underwent endoscopic retrograde cholangiopancreatography as a diagnostic test, 15 (10.0%) developed acute pancreatitis, 9 of whom required hospitalization.[21,22] The remaining 6 studies identified no harms related to screening.[14,15,17-20] The prevalence of incidental findings was not consistently reported in the available studies.

Six studies reported on the harms of surgery (n = 32 persons receiving surgery).[14,17,18,20,22,33] One study reported a stricture to the hepaticojejunal anastomosis in 1 patient 11 months after surgery and unspecified postoperative complications in another patient.[14] In another study, 2 cases of postoperative fistula and 3 cases of diabetes were reported.[17] Four studies reported no harms.[18,20,22,33]

Pancreatectomy carries a significant risk of morbidity and mortality, and additional data on the harms of surgery are available from studies not specifically conducted in screen-detected persons. A German study of 428 patients undergoing pancreatectomy (primarily pancreaticoduodenectomy) reported a 33.6% rate of any complication.[34] One 2003 US study reported a 4.6% rate of perioperative mortality after pancreatectomy for neoplastic disease,[35] and another US study of 21 482 pancreatectomies performed between 2007 and 2010 found a 3.7% 30-day mortality rate.[36]

Estimate of Magnitude of Net Benefit

The USPSTF considered the evidence using a reaffirmation process and found no new evidence on the benefits of screening for pancreatic cancer. The USPSTF found adequate evidence that the magnitude of the harms of screening for pancreatic cancer and treatment of screen-detected pancreatic cancer can be bounded as at least moderate. Therefore, the USPSTF reaffirms its previous conclusion that the potential benefits of screening for pancreatic cancer in asymptomatic adults do not outweigh the potential harms.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from February 5 through March 4, 2019. In response to public comment, the USPSTF added information on survival rates for pancreatic cancer by stage. The USPSTF added information about the consensus guidelines for the management of intraductal papillary mucinous neoplasms of the pancreas, and the accuracy (ie, sensitivity and specificity) of those guidelines in predicting the presence of pancreatic cancer or high-grade dysplasia. The USPSTF also added data on longer-term follow-up of screening studies in persons at high familial risk of pancreatic cancer. A few comments requested that the USPSTF make a recommendation on screening in persons with a history of familial pancreatic cancer or persons with an inherited genetic syndrome known to be associated with high risk of pancreatic cancer. In response, the USPSTF wants to clarify that these groups are outside the scope of this recommendation and that this recommendation does not apply to these persons.

Reaffirmation of Previous USPSTF Recommendation

This recommendation is a reaffirmation of the USPSTF 2004 recommendation statement against screening for pancreatic cancer in asymptomatic adults.[37] In 2004, the USPSTF reviewed the evidence on screening for pancreatic cancer and concluded that the harms of screening for pancreatic cancer exceed any potential benefits. For the current recommendation, the USPSTF commissioned a systematic review[12,13] to look for new evidence on the benefits and harms of screening. The USPSTF found no new substantial evidence that would change its recommendation and therefore reaffirms its recommendation against screening for pancreatic cancer in asymptomatic adults.

Recommendation of Others

No organization currently recommends screening for pancreatic cancer in the general population of asymptomatic adults. The American College of Gastroenterology conditionally recommends surveillance for pancreatic cancer in certain high-risk persons (eg, those with known genetic syndromes associated with pancreatic cancer and those from familial pancreatic cancer kindreds who have an affected first-degree relative) and suggests that surveillance should be performed in experienced centers, ideally under research conditions.[38]

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