JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2012;42(12)1219–1221
doi:10.1093/jjco/hys157
Advance Access Publication 5 October 2012

A Randomized Controlled Trial on the Efficacy of Thoracic CT Screening for Lung Cancer in Non-smokers and Smokers of <30 Pack-years Aged 50–64 Years (JECS Study): Research Design

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Received August 10, 2012; accepted September 7, 2012

In order to assess the efficacy of lung cancer screening using low-dose thoracic computed tomography, compared with chest roentgenography, in people aged 50–64 years with a smoking history of <30 pack-years, a randomized controlled trial is being conducted in Japan. The screening methods are randomly assigned individually. The duration of this trial is 10 years. In the intervention arm, low-dose thoracic computed tomography is performed for each participant in the first and the sixth years. In the control arm, chest roentgenography is performed for each participant in the first year. The participants in both arms are also encouraged to receive routine lung cancer screening using chest roentgenography annually. The interpretation of radiological findings and the follow-up of undiagnosed nodules are to be carried out according to the guidelines published in Japan. The required sample size is calculated to be 17 500 subjects for each arm.

Key words: lung cancer screening – computed tomography – efficacy – randomized controlled trial

INTRODUCTION

Lung cancer is the leading cause of cancer death in Japan as well as western countries. To decrease the lung cancer mortality, lung cancer screening using low-dose thoracic computed tomography (CT) may be a promising measure (1,2). Although there has been one report of a randomized controlled trial (RCT) in smokers (30 pack-years or over) demonstrating mortality reduction in the CT screening group (3), the efficacy of CT screening for lung cancer in non-smokers/smokers of <30 pack-years has not been reported so far. To demonstrate the efficacy in non-smoking subjects is very important, because non-smokers have recently been increasing in Western countries and lung cancer mortality even in non-smokers is considerably high.

In a recent Japanese cohort study, mortality reduction by thoracic CT screening was even suggested in non-smokers/smokers of <30 pack-years. Therefore, we are now conducting the JECS Study (The Japanese randomized trial for evaluating the Efficacy of low-dose thoracic CT Screening for lung cancer in non-smokers and smokers of <30 pack-years).

PROTOCOL DIGEST OF THE STUDY

PURPOSE

The aim of this study is to assess the efficacy of lung cancer screening tests using low-dose thoracic CT once every 5 years, compared with chest roentgenography (XP), in people aged 50–64 years with a smoking history of <30 pack-years.

Study Setting

This study is a multi-regional prospective RCT, with 6 participating centers and 11 municipalities in 5 prefectures in Japan as of 1 May 2012.

Endpoints

The primary endpoints of this trial are comparing the sensitivity and specificity of the screening modality for lung cancer between CT and XP performed in the first year of this study. The secondary endpoints are comparing the distribution of the stages of lung cancers, the diameter of lung cancers and the rate of advanced lung cancers, which are possible surrogate markers for mortality reduction. The potential risks of this screening, such as surgical resection, needle aspiration cytology or bronchoscopy for benign nodules, will also be identified and compared, by collecting further data on diagnostic procedures in all screening-positive cases. Although mortality reduction will be directly evaluated after a follow-up of 10 years, evaluating mortality reduction cannot be set as primary endpoint because of a short-term funding regulation.

Eligibility Criteria

The inclusion criteria are as follows:

(i) people aged 50–64 years when registered,
(ii) people whose smoking history is <30 pack-years,
(iii) people who received a lung cancer screening using chest XP in the previous year,
(iv) people who provide informed consent to participate in this study.

The exclusion criteria are as follows:

(i) people with a history of lung cancer,
(ii) people under investigation/follow-up due to a suspicion of lung cancer,
(iii) people with a history of a malignant disease other than lung cancer within 5 years,
(iv) people with a history of thoracic CT screening within 10 years,
(v) people in poor general condition, who are not expected to live for 5 years.

Screening Methods

After informed consent is obtained from each participant, the participants' eligibility will be confirmed. Then, the screening methods will be randomly assigned individually by the Assignment Center of the Japanese Study Group for Evaluating the Efficacy of Thoracic CT Screening (4,5).

The duration of this trial is 10 years. In the intervention arm, low-dose thoracic CT is performed for each participant in the first year and the sixth year. The participants in this arm are encouraged to receive annual routine lung cancer screening using chest XP in the other years.

In the control arm, chest XP is performed for each participant in the first year. The participants in this arm are encouraged to receive annual routine lung cancer screening using chest XP in the other years.

The interpretation of CT findings, especially determining whether some invasive diagnostic procedure should be adopted or not, and the follow-up of undiagnosed nodules are performed according to the 'Low-dose CT Lung Cancer Screening Guidelines for Pulmonary Nodules Management (6)' established by the Japanese Society of CT Screening. A positive rate of <5% is preferred. The interpretation of chest XP findings is performed according to 'The Manual of the Lung Cancer Screening (7)' section in the 'General rule for clinical and pathological record of lung cancer' published by the Japan Lung Cancer Society.

Statistical Considerations

The sample size was calculated on the hypothesis that thoracic CT is expected to improve the sensitivity to 95% in the CT group compared with 60% in the XP group. Assuming the detection rate of lung cancer by thoracic CT screening to be 320/100 000, 17 500 subjects in each arm are needed to achieve a 5% statistical significance with an 80% power. The same sample size is also required to detect a 60% mortality reduction after 10 years.

Acknowledgements

We are grateful to Dr Toshiya Sato for advising statistical analysis and to Ms Kazuko Yamamoto and Ms Kanoko Matsushima for their assistance. This protocol was approved by the Institutional Review Board of Kanazawa Medical University in 2009 and was registered on the University Hospital Medical Information Network Clinical Trial Registration (UMIN-CTR), Japan in 2011 (registration number: UMIN000005909). Details are available at the following address: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000006988&language=J. The members of the JECS Study Group are as follows: Headquarters: Dr Motoyasu Sagawa (Principle investigator), Dr Tomotaka Sobue, Dr Kenji Nishii, Dr Kenji Eguchi, Dr Tomio Nakayama, Dr Tomoshige Hayashi, Dr Takeshi Kobayashi, Dr Toshiya Sato, Dr Hiroshi Tanaka, Dr Masami Sato, Dr Katsuhiro Ichikawa, Dr Satomi Takahashi, Dr Chisato Hamashima, Dr Hiroshi Saito, Dr Takaichiro Suzuki, Dr Kyoko Sato, Dr Ryutaro Kakinuma, Mr Jun Misawa and Dr Makoto Tanaka. Regional Centers (From North to South): Miyagi Center: Dr Satomi Takahashi, Dr Chiaki Endo, Dr Akira Sakurada, Dr Takashi Kondo and Mr Tohru Kanno. Niigata Center: Dr Hiroshi Tanaka, Dr Maki Hosoi, Dr Tohru Hiura, Dr Akira Yokoyama and Dr Yuzo Kurita. Ishikawa Center: Dr Motoyasu Sagawa, Dr Takeshi Kobayashi, Dr Makoto Tanaka, Dr Tsutomu Sakuma, Dr Yoshinori Kibe, Mr Kozo Nishida, Mr. Satoru Mizukami, Mr. Kazuhiro Ikeda, Mr Tetsuo Matsunaga, Mr Kazuhiro

Miyazaki, Mr Mutsuhiro Sanada, Dr Katsuo Usuda, Dr Yuichiro Machida, Dr Masakatsu Ueno and Dr Nozomu Motono. Okayama Center: Dr Kenji Nishii, Dr Takeyuki Numata, Dr Takuo Shibayama and Mr. Shigeru Nakada. Kagoshima Center: Dr Masami Sato, Dr Kaoru Oketani, Dr Hirofumi Nakayama and Dr Ichiro Kanetsuki.

Funding

This study was supported in part by the Grant-in-Aid for Scientific Research from the Ministry of Health, Labour and Welfare, and the Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Conflict of interest statement

None declared.

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総 説

利益と不利益を考慮した肺癌検診のあり方

The ideal way of lung cancer screening to consider the balance of benefit and harm

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Abstract

The National Lung Screening Trial (NLST) as randomized-controlled trial that evaluated the effectiveness of the lung cancer screening to compare low dose CT (LDCT) with plain chest X-ray demonstrated annual LDCT reduced 20% of lung cancer mortality than annual plain chest X-ray. This study demonstrated the mortality reduction as the benefit of annual screening with statistically significant but reported 25% of positive rate and considerable number of death within 60 days after diagnostic workup and therapy as the harm of screening. The assessment of the study result is difficult in the meaning of comparison between benefit and harm of LDCT screening. The study result caused controversy about whether LDCT screening should be spread in the point of view of comparison of benefit with harm.

Keywords: screening for lung cancer, LDCT

肺癌検診については、低線量CT検診が注目されてきた。この検診手法は、従来の手法（胸部単純X線）では指摘できない小さくかつ淡い陰影を容易に指摘できることから、従来法の数倍の発見率、8割のI期率、約8割の生存率が報告され、世界的に注目されてきた。2011年6月に、ランダム化比較試験であるNational Lung Screening Trial (NLST) が報告された[1]。

この結果は、介入群の肺癌死亡率が対照群に比べて20％減少したという意味での利益を示したが、過剰な要精検率と、精密検査に関連した死亡という不利益も、同時に報告されており、その総合的な評価は困難になっている。

ここでは、NLSTの成績を中心に利益と不利益を考慮した肺癌検診のあり方について概説する。

1. NLSTのデザイン

NLSTは、喫煙者を対象とした年1回の低線量CTの効果を明らかにするため、全米33カ所で行われた大規模ランダム化比較試験である。2002年8月から2004年4月までの間に53,454人が登録され、研究群と対照群の2群に無作為に割り付けられた。研究群には登録時と年1回の低線量CTが計3回提供され、一方対照群には登録時と年1回の胸部単純X線検査が同じく計3回提供された。CTの"陽性"の定義として4mm以上の石灰化のない結節とし、3回目で同一の所見で変化がない場合は"陰性"とした。検診相終了

表1 National Lung Screening Trialの結果の要約（文献1より作図）

群	追跡人年	肺癌死亡数	肺癌死亡率（1/10万人年）	肺癌死亡率減少（%）
CT	144,097.6	354	245.7	20.3
CXR	143,363.5	442	308.3	

受稿2011年12月7日 受理2011年12月21日

表2 National Lung Screening Trialのスクリーニング判定結果（文献1より修正して引用）
プロトコール上4mm以上の結節を"Positive"とした。精密検査のルールについては、取り決めはしなかったが、治療や診断が必須なものを臨床的問題症例率として計上している

	低線量CT検診群				単純X線検診群			
	受診者数	Positive rate（%）	臨床的問題症例率（%）*	精検不要率（%）	受診者数	Positive rate（%）	臨床的問題症例率（%）*	精検不要率（%）
初回	26,309	27.3	10.2	62.4	26,035	9.2	3.0	87.8
2回目	24,715	27.9	6.1	65.9	24,089	6.2	1.8	92.1
3回目	24,102	16.8	5.8	77.3	22,346	5.0	1.5	93.4

表3 National Lung Screening Trialの診断・治療に伴う重篤な偶発症および死亡（文献1より修正して引用）

	低線量CT検診群					単純X線検診群				
	外科的生検	気管支鏡	針生検	侵襲的診断行わず	計	外科的生検	気管支鏡	針生検	侵襲的診断行わず	計
肺癌確定例										
精検総数	509	76	33	31	649	189	46	29	15	279
重篤な偶発症	71	2	0	2	75	22	1	0	1	24
60日以内死亡	5（1.0%）	4（5.3%）	1（3.0%）	0	10（1.5%）	4（2.1%）	5（10.9%）	1（3.4%）	1（6.7%）	11（3.9%）
肺癌非確定例										
精検総数	164	227	66	16,596	17,053	45	46	24	4,559	4,674
重篤な偶発症	9	2	0	1	12	1	0	0	3	4
60日以内死亡	2（1.2%）	4（1.8）	0	5（＜0.1）	11（0.1）	0	0	0	3（0.1%）	3（0.1%）

後5年間、電話と郵便で追跡された[2]。

2. NLSTの結果

表1に示すごとく研究群と対照群の死亡率の差は、63.4/10万人年であり、肺癌死亡率減少効果は20.3%と、統計学的有意に死亡率減少効果が示されている。これはNLSTのサンプルサイズ計算の際に仮定された効果の大きさ（20%）とほぼ一致しており、デザインどおりの効果が得られている。一方、検診の不利益としての要精検率の大きさについては、表2に示すように平均27%というとても大きな値が示されている。本研究では4mm以上を精密検査の対象と定義しておきながら、個々の症例について実際に精密検査を行うのか、診断へのステップ等については、各施設に一任されており、異常陰影が認められたうちのどれだけの割合が、実際に精密検査が行われたのかは公開されていない。また、診断治療の偶発症については（表3）、侵襲的診断法・治療の60日以内の死亡が報告されている。肺癌確定例で約1.5%というきわめて高い値が示されている。これらが本当に偶発症の範疇にあたるかどうかは、記載されておらず、診断治療とは無関係の死亡も含まれている可能性や、原病死の可能性もあるが、いずれにしてもきわめて高い値である。

3. 放射線被曝の影響と日本での現状

NLSTは、管電流20-30 mAsの低線量で撮影されている[2]。国内外で報告されている研究的な試みもすべて同様の低線量である[4]。この場合の被曝線量は、1.5 mSv程度の低線量であり、胃のX線検診（間接撮影）とさほど変わらない値である。一方日本人間ドック学会の調査によれば、低線量CT撮影ができている施設はわずか29.7%であり、診断レベルの通常線量撮影が多い（図1）[3]。あくまで検診は健常者を対象にしているものであり、診断用の線量を定期的に照射することは、リスクーベネフィットの観点から明らかに問題である。東日本大震災以降放射線被曝に対する国民の不安は極限に達しており、速やかな低線量化の普及が期待される。

4. 日本の精度管理指標の現状

日本CT検診学会の精度管理報告によれば（図2）、当初10.5%であった要精検率は低下し、2009年には

5.8％まで低下している。一方発見率・切除率・I期率も低下しているが、発見率の低下に比べて切除率・I期率はわずかで70-80％の範囲内で高い値を保っている。CT検診の場合、検診が開始された初期には、スリガラス状陰影（ground grass opacity: GGO）が陰影の大半を占めるpure GGOケースが積極的に外科的治療を受けていた。しかしこのようなケースは病理学的にも非浸潤がんや上皮内がんであり、過剰診断につながる可能性が高いことから、最近では経過観察のみにとどまるケースが多く、これらは病理学的診断がつかないため発見癌には含まれないので発見率の低下につながると考えられる。これはあながち精度の低下ではなく、検診の繰り返しにより適正化されてきたものと考えられる。

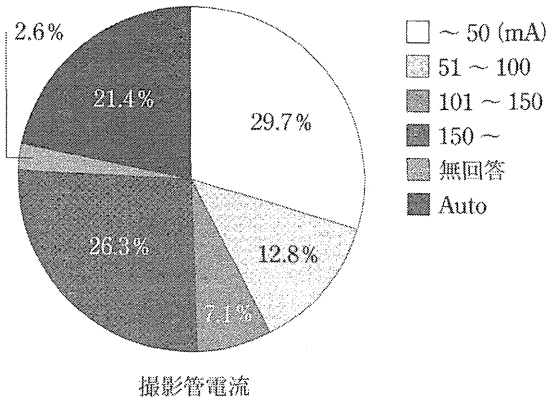

図1　国内でのCT検診実施状況
（文献3より修正して引用）撮影管電流50 mAs以下が低線量と定義されている

5. 国内での肺癌侵襲的診断法による偶発症

我が国での気管支鏡検査、経皮針生検による重篤な合併症（空気塞栓、呼吸停止、ショック、心停止）はそれぞれ0.03-0.05％、0.05-0.06％と報告され、また検査に伴う死亡率はそれぞれ0.01-0.02％、0.07％と報告されている[4]。これらは検査直後のものにおおむね限られており、NLSTの60日以内という条件とは異なるものの、あまりにもかけ離れた成績である。技術的な問題というよりも、対象者の心肺機能（COPD、間質性肺炎、動脈硬化性疾患など）等に大きな問題があったのではないかと推察される。国内の状況では偶発症という不利益は比較的小さいと考えられるものの、胃・大腸癌等に比べれば大きな値であり、対象者への十分な説明は不可欠である。

6. まとめ

NLSTの成績は、低線量CT検診の年1回の受診により喫煙者の肺癌死亡率を20％減少することができたという利益を示している一方、要精検率の高さと診断・治療関連死の多さという不利益も高いということを示しており、普及すべきかどうかの判断が困難である。日本ではすでに約20万人程度の年間CT検診受診者があり、その精度管理は適正化され、精密検査や

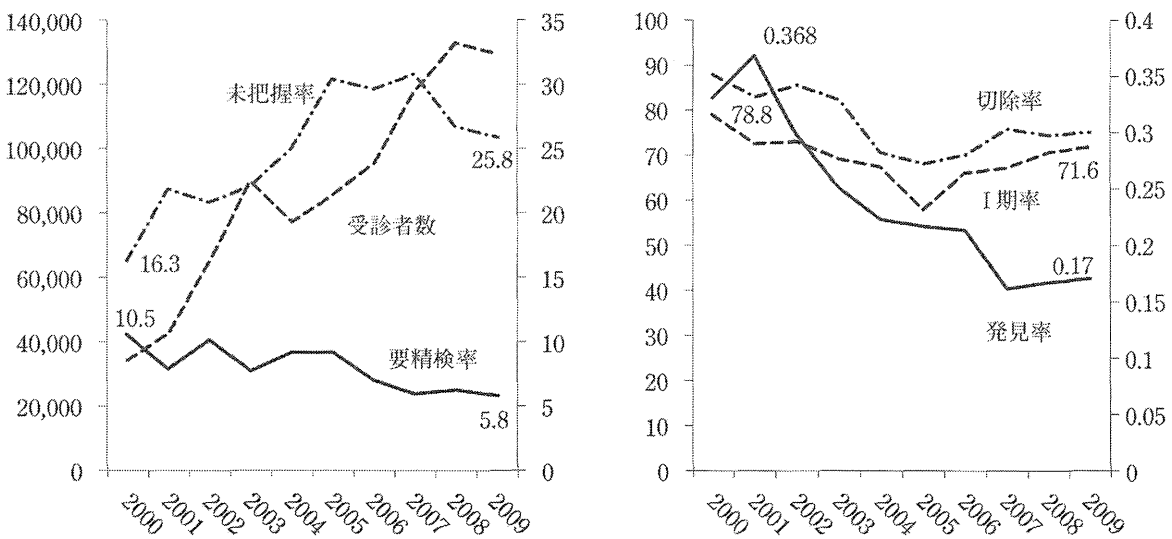

図2　CT検診の精度管理指標の推移（日本CT検診学会精度管理部会全国集計より作図）

手術による重篤な偶発症の率も米国に比べてかなり低く、安全性は担保されているように思われるが、一方で診断線量でのCT撮影を行う人間ドックも決して少なくない。人間ドック従事者に対する基本的な知識と情報の普及が十分でなく、今後の対応が期待される。

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要旨

日本がん検診・診断学会誌 19(3) : 266-269、2012

年1回の低線量CTを用いた肺癌検診の有効性を評価したランダム化比較試験National Lung Screening Trialが、単純X線検査受診群に比べて約20%の肺癌死亡率減少効果があることを示した。この研究では、死亡率減少効果という利益を統計学的有意に示したものの、25%という高い要精検率と精密検査・治療後60日以内の死亡数が無視できないという不利益についても報告している。利益と不利益の大きさを比較し、CT検診の普及が適切かどうかを判断するには難しい研究結果であった。

わが国では年間20万人程度のCT検診受診者があり、要精検率も当初の10.5%(2001年)から5.8%(2009年)に低下していると報告されている。また肺癌診断・治療に伴う偶発症は国内では0.001%と程度と報告されている。一方で人間ドックを対象とした調査においては、低線量で撮影している施設は29.7%に過ぎないという調査結果もある。海外での研究結果を日本に外挿できるかどうかという点では、二次予防に関与するすべての医師への知識の正確な普及が鍵となる。

キーワード：肺癌検診、低線量CT

原 著

低線量胸部CTを用いた肺がん検診の有効性評価のための日本における無作為化比較試験の現況と課題

佐川元保、西井研治、祖父江友孝、江口研二、中山富雄、佐藤雅美、小林 健、田中洋史
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細井 牧、佐藤恭子、柿沼龍太郎、三澤 潤、田中 良、遠藤千顕、桜田 晃、近藤 丘
菅野 通、樋浦 徹、横山 晶、栗田雄三、佐久間 勉、木部佳紀、西田耕造、水上 悟
池田一浩、松永哲夫、宮崎一弘、眞田睦博、薄田勝男、町田雄一郎、上野正克、本野 望
沼田健之、柴山卓夫、中田 茂、中山博史、鐘撞一郎、小林弘明、大森淳子

【背 景】 喫煙指数600未満の住民に対する低線量胸部CTによる肺がん検診の有効性を評価するために、無作為化比較試験を現在日本で実施中である。
【方 法】 50～64歳で喫煙指数600未満の男女のうち前年の胸部X線による肺がん検診を受診した住民を対象にこの研究への参加者を募る。参加者を無作為に2群に振り分け、CT群には1年目と6年目に低線量胸部CTを提供し、XP群には1年目に胸部X線を提供する。それ以外の年には、両群とも10年目まで通常の住民検診での胸部X線を受診することを勧める。
【結 果】 2012年3月までに1,547名の住民が参加資格ありと判定され、研究への勧誘文書が送られた。そのうち412名が説明会に参加し、396名（26%）が研究に登録した。
【結 論】 この研究の勧誘への承諾率は、類似の研究での承諾率に比較して相当高いものであった。

キーワード： 低線量胸部CT、肺がん検診、有効性評価、無作為化比較試験
J Thorac CT Screen 2012; 19: 196-203

はじめに

肺癌は本邦のがん死亡の1位となり、非喫煙者の腺癌も増加しているため、喫煙対策と並んで検診の重要性も増大している。胸部CT検診は早期肺癌を高率に発見できるが、肺癌死亡減少効果は完全に確立しているとは言えない。特に非喫煙者・低喫煙者における肺癌死亡減少効果に関しては、ほとんどエビデンスが存在しないのが現状である。本邦では、死亡減少効果に関する確たるエビデンスのないままCT検診が広がってきているが、任意型検診であればともあれ、行政レベルで行う対策型検診として導入する際にはしっかりしたエビデンスが必要である。今回我々は、無作為化比較試験によりCT検診の有効性を評価する研究を計画し現在実施しつつあるので、その現状と課題を報告する。

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がん検診の有効性評価

多くの報告[1, 2]で示されているように、胸部CTは肺癌を早期に発見可能であり、発見肺癌の生存率はきわめて良好である。しかしながら「肺がん検診」として有効か、すなわち「肺癌死亡を

減らせるか」は別の問題である。その理由は、検診発見例にはバイアスが存在するために、発見率や生存率では適切に評価することが困難だからである。

一例としてLead-time biasと呼ばれるバイアスを挙げる。これは、検診で発見された癌は、症状が出現する前に発見されたのであるから、症状が出現してから診断される「症状発見群」に比較して、症状が発現するまでの期間分長生きする、というバイアスである。検診で見つかるより症状が出るまで2年かかるとすると、検診発見例は症状発見例よりもまったく予後が改善しなくとも、生存期間は必ず2年延長することになる。このように、生存期間や生存率では適切に評価することが困難なので、受診者または対象者全体の肺癌死亡率の低下を示す必要がある。

有効性評価研究では、採用した研究方法がバイアスをどの程度制御できるかにより信頼性に大きな差が存在する。無作為化比較試験が最も信頼性が高く、症例対照研究とコホート研究がそれに次ぐ。地域相関・時系列研究は信頼性が低く、モデル解析はさらに低い。バイアスや研究方法の詳細については触れる余裕がないので他稿[3]を参照いただきたい。

確実とはいえなくとも良いかもしれない方法があるのに、なぜ推奨しないのか？

対策型（住民検診型）検診として推奨されるためには「死亡を減少させる」証拠が必要だが、そこまで厳密に考えなくとも「良いかもしれない方法があれば採り入れれば良いのでは？」と思われる医療関係者もいると思う。ある面でそれは自然な考え方でもある。

実際にある新しい検診を採用するかどうか決める場合、2つのタイプの誤りが起こり得る。①本当は有効なのに採用せず死亡者が増える、②本当は無効なのに採用して不要な検査をしたあげく死亡を含む不利益を受ける人を作る、の2つである。「効果が確定していない」状況では、どちらも避けるような選択肢はなく、どちらかの危険は許容せざるを得ない。臨床の立場で患者さんが外来に来たときを想定すると、実際に病んで医師を受診した患者さんに対して、確実でないからといって何もしないより、無効かもしれないけど何かしてあげたい、すなわち①を避けて②を許容することが多いと思う。しかし、検診では健常者、すなわち何もしなければ元気だった人を対象としているので、そのような人に不利益を与えること、すなわち②は絶対に避けることこそが第1に必要なことである。そのために「死亡率減少の確認」がされないうちは採用できないのである。

本邦ではかつて神経芽細胞腫の検診が行われていた。現在は死亡率減少効果が明らかでないとされ中止されているが、行われていたころの統計[4]では1,226例が手術され、そのうち8例が手術の合併症により死亡している。また、そのほかに10例が化学療法の合併症により死亡している。死亡例の中には、本来は自然退縮していたはずの腫瘍もあったかもしれない。これからは、我々が新たな検診を採用する場合には「このような結果が確定したから採用した」と後の時代に説明できるような、少なくとも後に誤りを検証できるようなルールで行う必要がある。「良い結果が出そうだ」という程度では採用できず「良い結果が出た」が必要なのである。

低線量胸部CT検診の有効性評価のための無作為化比較試験（RCT）計画の初版とその改訂に至る経過

2008年に厚生労働省垣添班が組織され、CT検診に関するRCT計画の立案が企画された。著者らを中心に2009年にRCT計画書の初版を策定・上梓したが、初版では喫煙者・非喫煙者の両者を対象とした計画を立案した。詳細は他稿[5～7]に譲るが、概略としては50～64歳の現行

肺がん検診受診者男女を対象として、対照群では全員現行検診を10年間、研究群では喫煙の有無によって検査の種類が異なり、喫煙者では低線量CT検診＋喀痰を10回、非喫煙者では低線量CT検診は1、3、7年目の3回で残りは現行検診を行う、というデザインであった。効果の有無が不明であるのだから、検診費用はすべて研究費でまかない自己負担は無しとした。対照群に割り付けられた場合「CTによる内臓脂肪測定と生活習慣病に関する大規模前向きコホート研究」に参加できるというオプションを付けた。肺癌死亡減少効果を評価するために必要な研究参加者数は5万人、研究費用は年間2億3,000万円余、15年の研究期間の総額で35億円余と算定された。その計画に基づき予算申請を行ったが本体の計画は採用されなかったため、2010年から一部地域でパイロット研究として開始した。

2010年秋にNLSTの研究[8]が報告され、研究計画の練り直しが必要とされた。その理由として、

① NLSTの結果は、要精検率が高すぎるなどの問題はあるものの、喫煙者に対しては死亡率減少効果があるという報告であることは間違いない。

② 1報のみでは「結果は確定的」と断ずるのは難しいが、ヨーロッパで行われているNELSON[9]の結果も「効果あり」となれば、喫煙者に対しての効果はほぼ確立したと考えられるだろう。

③ NELSONの結果が「効果なし」だと評価は困難になるが、ヨーロッパでは他にもいくつものRCTが実施されており[10,11]、それらの結果を統合すればそれなりに結論が出ることが推測される（ただし、「効果あり」となっても、対策型検診に導入されるためには、高い要精検率などの「不利益」や「コスト」の問題が残るので簡単ではない）。

④ 今から喫煙者のRCTを日本で組んでも、すでに多数のRCTが欧米で走っており、周回遅れ・2周遅れといってよい状況であるため、巨額の費用と膨大な作業を費やす意義を見出すことが困難になってきた。

⑤ 非喫煙者では死亡減少効果はまったく不明であり、欧米ではむしろ現在のところ否定的なイメージが強く、有効性評価研究の計画すらない。しかし、非喫煙者のほうが喫煙者よりもCT検診受診による相対危険度の低下が大きかったという中山班コホート研究の結果（厚生労働科学研究費補助金第3次対がん総合戦略研究事業：低線量らせんCTを用いた革新的な肺がん検診手法の確立に関する研究報告書参照）が公表されれば、必ず欧米でRCTが組まれるだろう。

⑥ 最大の外的要因として、使用できる予算が少なく、日本の景気や国家予算の動向を鑑みれば、その状況が10年以内に改善する可能性も高くないため、原計画のままでは、計画通りに完遂することはほぼ不可能と考えられる。

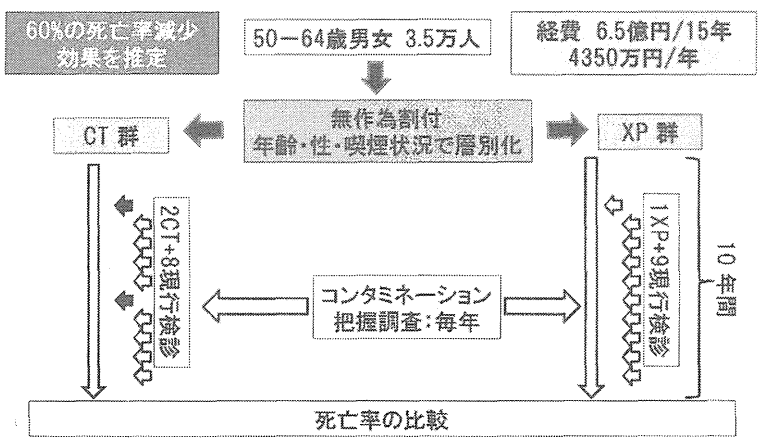

Fig. 1 厚労省佐川班 低線量CTによる肺がん検診のRCT（喫煙指数600未満のみ）

以上のような現状を踏まえ、本邦で行うべき研究として非喫煙者および低喫煙者における有効性の検証に重点を置いて、計画を改訂することにした。

低線量胸部CT検診の有効性評価のための無作為化比較試験（RCT）計画改訂版

2011年改訂版の内容は以下の如くである(Fig. 1)。

① 現行肺がん検診の前回受診者のうち喫煙指数が600未満である50～64歳男女に対して個別にこの研究への勧誘文書を郵送し、無作為化や被曝、予後調査、不利益を含めた十分なインフォームドコンセントを得たうえで、研究参加を募る。

② 検診受診者から勧誘する意味は、最も大きな交絡因子である直近の検診受診の有無を揃えられること、検診に対する意識が高く研究参加を募りやすいこと、高いコンプライアンスが期待できること、胸部X線との相対危険度を算出する必要があるため対照群の胸部X線（通常の住民検診）受診のコンプライアンスも高い必要があること、などのためである。

③ 研究参加募集に応じた者に対して、年齢・性・喫煙状況（非・低喫煙）・地域が大きく偏らないよう調整した無作為化により、半数には胸部CTを、残りの半数には胸部X線を撮影する。

④ 胸部X線受診群には、受診者が希望すればCTによる内臓脂肪測定を含むコホート研究に参加することができるオプションを加える。

⑤ 2年目以降10年目までは両群とも通常の住民検診を受けるよう勧めるが、胸部CT群では6年目にもCT検診を提供する。

⑥ 10年間の予後をフォローし、肺がん罹患・死亡を把握することによりCT検診の感度・特異度を算出し、さらに死亡率減少効果を評価する。

⑦ 非・低喫煙者に対するCT検診の効果は高喫煙者に対するよりも大きいと想定されたため、死亡率減少効果をX線検診に比較して60%減少と見込むことができた。それにより、必要参加者数を35,000人まで減少させた。

⑧ 必要参加者数の減少、非・低喫煙者が対象のためCT検診を毎年行う必要はなく検診間隔を長くできること、検診の一部を住民検診に代替してもらうこと、などにより必要な経費を大幅に削減することができ、研究費用は年間4,000万円余、15年の研究期間の総額で6億円余と算定された。現在交付されている額は、この額の半分以下であり十分とは言えないが、以前の計画では必要予算の1/10以下しか交付されなかったことから見れば、実現可能性ははるかに高まった。

⑨ 参加者の予後は最低でも10年間フォローする必要がある。職場検診のフィールドを用いる場合は、退職などにより長期間のフォローが不可能になる場合が少なくない。そのため、フィールドの候補としては市町村を第1に念頭に置く。

これまでの研究実施の概要（Fig. 2）

2010年度は石川県（担当：石川県立中央病院・小林　健、金沢医科大学・田中　良）では羽咋市で、岡山県（担当：岡山県健康づくり財団附属

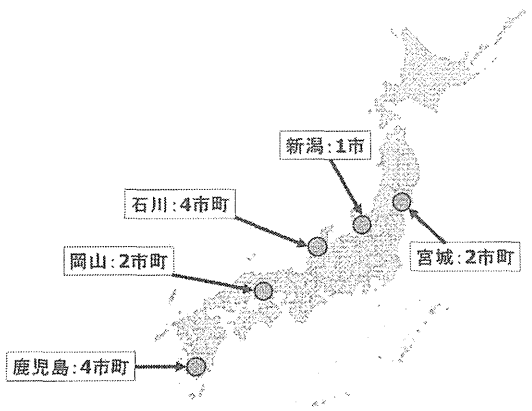

Fig. 2　佐川班RCT地区（2012年12月現在）

病院・西井研治）では里庄町で研究を開始、2011年度は新潟県（担当：新潟県立がんセンター新潟病院・田中洋史）では新潟市西蒲区、鹿児島県（担当：鹿児島大学・佐藤雅美、鹿児島県民総合保健センター・桶谷　薫）では指宿市で研究を開始した。2012年度はさらに石川県、鹿児島県、岡山県、宮城県（担当：宮城県立がんセンター・高橋里美、東北大学・遠藤千顕、桜田晃）、福井県（担当：福井県済生会病院・小林弘明）で合わせて新たに10地区での開始が決定しており、ほかにこれまで未実施の県も含めた数市町村で開始に向けて準備中である。

実際の研究における説明会と検診の当日の流れは、Fig. 3およびFig. 4に示すようなものが標準的だが、説明会と別の日に検診を行う場合や、X線群に内臓脂肪コホート調査を行わない場合などもあり、地域の実情に応じて改変して行っている。

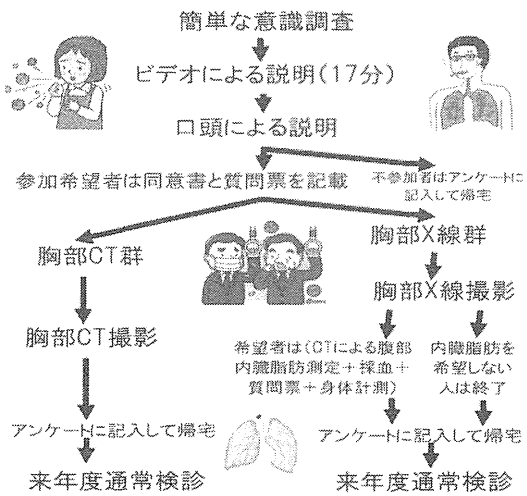

Fig. 3　標準的なパターンでの当日の流れ

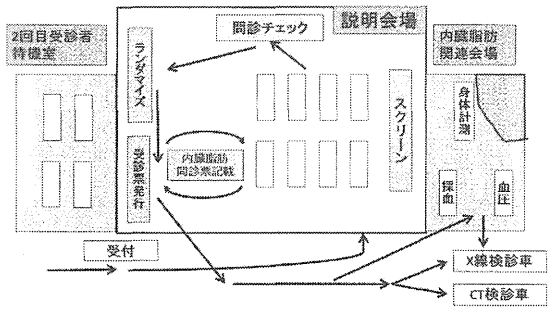

Fig. 4　当日の配置の例

これまでの結果の概略

2011年度までに実施した結果を概括すると、4市町で合わせて1,547名に勧誘文書を郵送し、440名（28%）が説明会参加を希望し、実際に説明会に参加したものが412名（全体の27%、参加希望者の94%）、研究に参加したものが396名（全体の26%、説明会参加希望者の90%、説明会参加者の96%）となった。

説明会参加者を対象に、事前勧誘・説明書および説明会の理解度調査を実施した。解析は現在行っているところであるが、最初の2市町（羽咋市・里庄町）の結果では、事前の勧誘・説明書の内容はおおむね80～90%の参加者が理解できていたが、説明会の後にはほぼ100%まで上昇することが判明した（Fig. 5）。研究目的・研究期間・研究方法・検診の不利益・精密検査の不利益・検診の限界・研究に参加するための費用・事後調査・同意の撤回・結果の公表の10項目にわけて内容の理解度を調査すると、「検診の不利益」と「精密検査の不利益」の項目の理解度がやや低く90～95%程度で、他の項目はほぼ100%であった。

研究参加者を対象に、主に検診受診に伴う

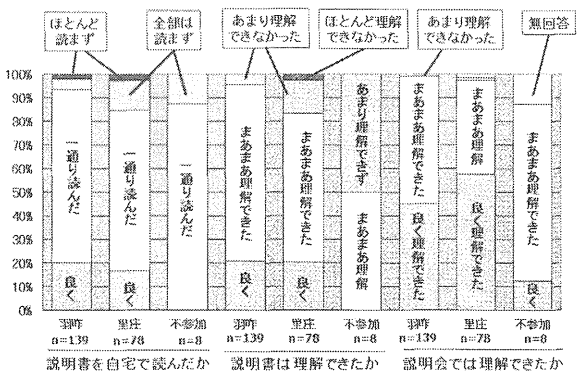

Fig. 5　研究全般の理解度

「不安感」の増大に関する不利益の有無を評価するためのQOL調査と、コンタミネーション（予定外の当該がんの検診、すなわち本研究での検診および現行検診以外の検診目的の検査）の調査のために年に1～2回の郵送による調査を行っている。初年度の石川県羽咋市でのコンタミネーションの暫定結果は10％以下と少ない水準であった。

考　察

本研究はまだ開始してわずかの期間しか経過していないため、解析できる内容は限られているが、それでも本研究の対象者の1/3～1/5、平均で28％が説明会参加を希望し、実際に研究に参加した者は説明会に参加した者の9割、対象者全体の26％と高率であることが判明した。同様の肺がん検診に関する無作為化比較試験の応諾率と比較すると、PLCO研究では0.3～7.2％[12]、ITALUNG研究では4.5％[10]と報告されており、本研究の応諾率はきわめて高い。その理由としては、前回の現行肺がん検診受診者に勧誘を行ったことにより、肺がん検診に興味のある集団を対象としたこと、喫煙歴が判明しているため勧誘対象を絞り込めたことなどのほかに、対照群に内臓脂肪測定のオプションを付けたために対象者の興味を得やすくなったことも大きな要因と考えられる。また、説明会参加者の9割が実際に研究に参加しているが、このことは、① 説明会参加後に「不参加」と決断する参加者が少ない、② 説明会参加後に「不適格」になる参加者が少ない、ということが言え、今回作成・配布している勧誘・説明書は、① 研究内容の適切な伝達、② 不適格例の排除、の両面において有効に機能していると考えられた。

対象者の約1/4が研究に参加する、ということは、かなり効率よく研究を進めることが可能、ということでもある。しかしながら、実際には各市町村が特定健診や介護保険で忙殺されているため、自治体の協力を得られるかどうかが最も重要なポイントになっており、今後も継続的な働きかけが必要となっている。このような研究に関する、もう1レベル高い国の支援があれば実現可能性は高くなるが、当面は研究者の地道な努力で地区を増やしていくしかない可能性が高い。本研究は35,000人の参加が最終的な目標であるが、第1段階の目標としては3,000人程度と考えており（欧米のいくつかの小規模RCTではその規模である）、そこまでは数年以内に到達できると考えている。

本研究の一部は、厚労省科学研究費補助金（第3次対がん総合戦略研究事業）および文部科学省科学研究費による補助金をもとに行われた。

本研究：JECS Study (the Japanese randomized trial for evaluating the efficacy of low-dose thoracic CT screening for lung cancer) に参加しているメンバーは以下の通りである。

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Present and future of a randomized controlled trial in Japan evaluating the efficacy of lung cancer screening using low-dose thoracic CT

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The Study Group of the Japanese Randomized Trial for Evaluating
the Efficacy of Low-dose Thoracic CT Screening for Lung Cancer
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Abstract

Background: A randomized controlled trial is now being conducted in Japan to evaluate the efficacy of lung cancer screening by low-dose thoracic computed tomography (CT) among people with a smoking history less than 30 pack-years.

Methods: Participants in the trial were recruited from residents, who were 50-64 years old with a smoking history less than 30 pack-years and underwent regular lung cancer screening using chest roentgenogram (CXP) in the previous year. The participants were randomly assigned into 2 groups (CT group and XP group), and low-dose thoracic CT was provided in the first and the sixth year for each participant assigned to the CT group, whereas CXP was provided in the first year for each participant assigned to the XP group, and all participants are encouraged to receive routine lung cancer screening using CXP annually for 10 years.

Results: As of March 2012, 1547 people from 4 municipalities in Japan were regarded as potential candidates and recruitment letters were sent to them. Of those candidates, 412 attended a meeting for explanation and recruitment to the study. Finally, 396 people (26%) participated in the study.

Conclusion: The compliance of recruitment in the study was considerably high, in comparison to other similar trials.

Key words: Low-dose thoracic CT, Lung cancer screening, Efficacy, Randomized controlled trial
J Thorac CT Screen 2012; 19: 196-203

Lung Cancer 78 (2012) 225–228

Contents lists available at SciVerse ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

A decrease in lung cancer mortality following the introduction of low-dose chest CT screening in Hitachi, Japan

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ARTICLE INFO

Article history:
Received 6 June 2012
Received in revised form 9 September 2012
Accepted 20 September 2012

Key words:
Computed tomography
Chest
Ecological studies
Lung cancer
Screening

ABSTRACT

Recent US clinical trial demonstrated that CT screening prevents lung cancer death among high risk individuals. However, it remains unclear whether wide implementation of low-dose CT screening for lung cancer can decrease mortality in the community. Among residents in Hitachi City (Japan), where nearly 40% of inhabitants aged 50–69 years were estimated to have participated in the screening at least once from 1998 through 2009, the trend of lung cancer mortality was described in relation to the timing of implementation of the CT screening. Cancer mortality data were obtained from regional cancer registry and standardized mortality ratio (SMR) of lung cancer was calculated for each 5-year period during 1995–2009. In both men and women aged 60 years or older, age-specific lung cancer mortality rates were generally lower during 2005–2009 as compared with those during 1995–2004. For combined men and women aged 50–79 years, SMR was nearly unity prior to or during introductory phase of CT screening and during early period of implementation; however, it was significantly decreased during 2005–2009, well after the implementation of CT screening, with SMR (95% confidence interval) being 0.76 (0.67–0.86). Results suggest that wide implementation of low-dose chest CT screening may decrease lung cancer mortality in the community 4–8 years after introduction of the screening.

1. Introduction

Screening for lung cancer using low dose computed tomography (CT) can detect smaller size of lung nodule than can chest radiography and thus has been expected to decrease lung cancer mortality. In June 2011, the National Lung Screening Trial (NLST) study group reported a 20% reduction in lung cancer mortality among persons randomly allocated to low dose CT screening compared with controls [1]. Based on a systematic review including the NLST study, the American College of Chest Physicians (ACCP) and the American Society of Clinical Oncology (ASCO) have released a clinical practice guideline, in which CT screening for lung cancer is recommended for high risk individuals [2]. In Japan, where CT screening for lung cancer was initiated first in the world [3] and has been implemented at community and workplace settings [4], evidence on the effectiveness of the CT screening is sparse and thus research is required to elucidate whether CT screening for lung cancer can decrease mortality.

Hitachi (Ibaraki prefecture), where low dose CT screening for lung cancer was initiated in the workplace in 1998 [5,6], is among areas with the largest number of the screening performed in Japan. Using data from a follow-up survey of 210 patients with lung cancer, 85% of which were on stage IA, detected on CT screening at Hitachi Medical Center and Hitachi Health Care Center, we reported an excellent survival (5-year survival of 90%) of these patients [7]. As of March 2006, nearly 30% of Hitachi citizens aged 50–69 is estimated to have received at least one CT lung cancer screening at either of the two medical facilities [7]. It would thus be of interest

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http://dx.doi.org/10.1016/j.lungcan.2012.09.012

Table 1
The number of participants in low-dose chest CT screening in the two facilities[a] in Hitachi, Japan (as of March 2009).

Age (year)	Men	Women	Total
50–54	10,108	5131	15,239
60–64	6223	6363	12,586
70–74	1775	1826	3601
80 or older	167	146	313
Total	18,273	13,466	31,739

History of smoking: men 74.1%, women 8.3%; total 46.2%.
[a] Hitachi Health Care Center and Hitachi Medical Center.

whether CT screening for lung cancer had any impact on mortality at community level. Here, we report the trend of lung cancer mortality among Hitachi citizens in relation to the timing of screening implementation.

2. Materials and methods

In Hitachi Health Care Center (Hitachi Ltd., Hitachi), chest CT screening for lung cancer has been conducted for ages 50–69 years for employees, retired persons, and their spouse since in 1998. In Hitachi Medical Center (Hitachi) also initiated chest CT screening for lung cancer for community dwellers aged 50 years or older in 2001. Details of the screening procedure, the numbers of participants and patients with lung cancer, and clinical features of screen-detected cases in each facility have been described elsewhere [5–7].

Table 1 shows the number of participants of the chest CT screening by sex and age as of March 2009. A total of 31,739 participants received the screening at least once (total 83,342 screenings, mean 2.6 times) at Hitachi Medical Center or Hitachi Health Care Center. The majority of the participants (men 89%, women 85%) were in ages 50–69, with the mean age of all participants being 57 years. Because we did not obtain information on address of screening participants, we assumed that the proportion of Hitachi residents among total screening participants was the same as that among participants with screen-detected lung cancer (76%). Based on this assumption, 36% Hitachi residents aged 50–79 (men 43%, women 30%) and 40% Hitachi residents aged 50–69 (men 47%, women 33%) were estimated to have received the screening program as of March 2009. Of these, 14,661 were current or past smokers, and more than a half (54%) had never smoked cigarette in their lifetime.

First, we examined time trend of lung cancer mortality and incidence in Hitachi. For this purpose, we obtained from the Ibaraki Cancer Registry data on lung cancer death and incidence by sex- and 5-year age-group for each Hitachi City and Ibaraki prefecture each year from 1995 to 2009 (1995 to 2007 for incidence). We also collected sex- and age-specific population statistics, which were derived from residential registry, in Hitachi City during the same period. Using these data, we calculated lung cancer mortality rate and its exact 95% confidence interval, based on the binomial distribution, by sex and 10-year age group in Hitachi City for three 5-year periods (1995–1999, 2000–2004, 2005–2009), each representing "stage of no or the beginning of CT screening program", "early stage of implementation", and "later stage of implementation".

Next, we compared the lung cancer mortality in Hitachi City with that for overall Japan. We first calculated the expected number of death from lung cancer by multiplying the sex- and age (5 years interval)-specific number of residents in Hitachi City by their corresponding mortality rate of lung cancer in Japan, and then summed. We then calculated standardized mortality ratio (SMR) as the observed number of death divided by the expected number of death as well as its exact 95% confidence interval based on the Poisson distribution. We repeated this analysis by using sex- and age-specific mortality data of Ibaraki prefecture. We also calculated age-standardized incidence rate of lung cancer in Hitachi for each year from 1995 to 2007 (standard population, the 1985 model population of Japan). All analyses were done with Stata version 10.1 (StataCorp, College Station, TX).

3. Results

Table 2 shows lung cancer mortality rate for each 5-year period by sex and age group. In men between ages 60 and 74, lung cancer mortality was slightly lower during the second period of 2000–2004 (early stage of CT screening), whereas it showed a large reduction during the third period of 2005–2009 (stable stage of CT screening) as compared with that during 1995–1999 (no CT screening or its introductory stage). Men aged 75–79 also showed a large reduction in mortality in the third period. Similarly, women aged 60 or older showed a decreasing trend of lung cancer mortality during the course of time.

Fig. 1 shows the time trend of age-standardized lung cancer mortality ratio (ages 50–79 year) for men and women combined in Hitachi using sex- and 5-year age group-specific lung cancer mortality statistics of whole population of Japan for calculation, together with that of age-standardized lung cancer incidence rate (ages 50–79 year). This analysis was limited to those aged 50–79 years, the majority (>99%) of CT screening participants in Hitachi. During the period of 1995–1999, when CT screening was not provided or has just introduced in Hitachi area, lung cancer mortality was comparable to that of national and prefectural levels; SMR (95% CI) was 0.95 (0.83, 1.08). There was also no material difference in mortality during the second period representing early stage of CT screening implementation; SMR (95% CI) was 0.97 (0.86, 1.09). During the third period (2005–2009), which corresponds to 4–8 years after the implementation of CT screening in both medical facilities in Hitachi, we observed a statistically significant, 24% reduction in lung cancer mortality; SMR (95% CI) was 0.76 (0.67, 0.86). Similar results were obtained when sex- and age-specific lung cancer mortality data of Ibaraki prefecture were used in calculating the expected number of lung cancer death in Hitachi; SMR (95% CI) was 1.04 (0.91, 1.17), 1.04 (0.92, 1.16), and 0.79 (0.69, 0.89) for 1995–1999, 2000–2004, and 2005–2009, respectively. In contrast, age-standardized incidence rate of lung cancer in Hitachi appears to increase after the introduction of CT screening in Hitachi Health Care Center (1998) and Hitachi Medical Center (2001).

To further examine which sex- and age-group showed reduction in lung cancer mortality, we repeated the above analysis for each sex- and/or age (10-year interval)-group using sex- and age (5-year interval)-specific lung cancer mortality of overall Japan (Table 3). For all the three age groups combined, a statistically significant decrease in SMR during the third period of 2005–2009 was observed in both men and women (men 24%, women 26%). A statistically significant decrease in lung cancer mortality was observed during the third period in men in 60s (32%), men in 70s (24%), and women in 70s (33%). Women in 60s also showed a decrease (25%), albeit statistically non-significant, in lung cancer mortality during that period.

4. Discussion

In the present study, we examined chronological changes of lung cancer mortality among residents of Hitachi City, where chest CT screening has been widely implemented as a community preventive service. As a result, we found a significant reduction in lung cancer mortality among target age groups 4–8 years after introduction of CT screening.

Table 2
Lung cancer mortality rate by sex, age, and period in Hitachi, Japan.

Age (year)	Period	Men			Women		
		Lung cancer death	Total population[a]	Lung cancer mortality rate (95% CI), per 100,000	Lung cancer death	Total population	Lung cancer mortality rate (95% CI), per 100,000
50–79	1995–1999	194	155,034	125 (108, 142)	57	166,975	34 (26, 44)
	2000–2004	228	169,910	134 (117, 153)	57	179,002	32 (24, 41)
	2005–2009	203	187,636	108 (94, 124)	53	194,686	27 (20, 36)
50–59	1995–1999	24	75,647	32 (20, 47)	11	74,608	15 (7, 26)
	2000–2004	31	71,952	43 (29, 61)	9	74,167	12 (6, 23)
	2005–2009	29	70,589	41 (28, 59)	10	71,128	14 (7, 26)
60–69	1995–1999	75	53,376	140 (111, 176)	18	53,451	34 (20, 53)
	2000–2004	80	66,153	121 (96, 150)	19	63,347	30 (18, 47)
	2005–2009	61	72,528	84 (64, 108)	18	73,492	24 (15, 39)
70–79	1995–1999	95	26,011	365 (296, 446)	28	38,916	72 (48, 104)
	2000–2004	117	31,805	368 (304, 441)	29	41,488	70 (47, 100)
	2005–2009	113	44,519	254 (209, 305)	25	50,066	50 (32, 74)

CI, confidence interval.
[a] The sum of the population each year.

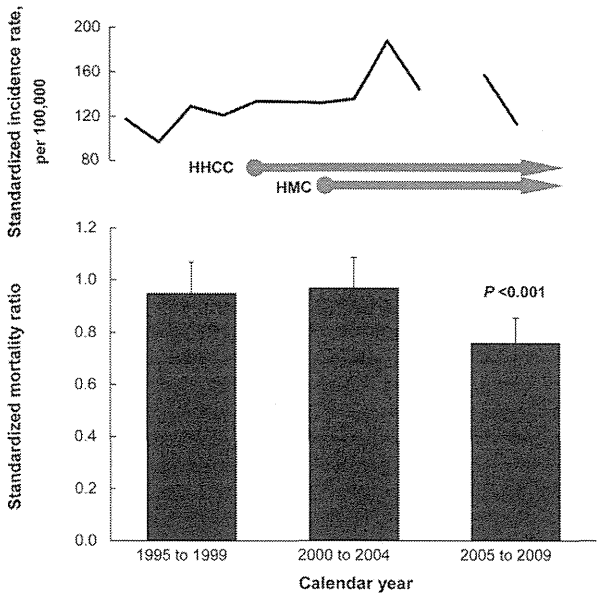

Fig. 1. Time trend of standardized mortality ratio (based on sex- and age (5-year interval)-specific lung cancer mortality in Japan) and standardized incidence rate (standard population is the 1985 model population of Japan. Data for 2005 is not shown due to a flaw in registration system) of lung cancer among residents aged 50–79 years in Hitachi, Japan. HHCC, Hitachi Health Care Center; HMC, Hitachi Medical Center. Arrows indicate implementation period of CT screening. Error bar indicates 95% confidence interval.

A recent finding from NLST provided strong evidence supporting the effect of low-dose CT screening in decreasing lung cancer mortality among those with a history of smoking [1]. Protective effect of the CT screening on lung cancer mortality was also supported from a prognostic investigation of patients with lung cancer detected on CT screening in the US [8]. Similarly, we previously reported an excellent long-term survival of patients with lung cancer detected on the CT screening in Hitachi area [7]. Lung cancer mortality in a cohort of smokers who received CT screening for lung cancer in New York State was compared with two unscreened cohorts (CPS-II and CARET), with adjustment for age, sex, and smoking history [9]. The authors found a significant reduction of deaths from lung cancer (36% and 64% for CPS-II and CARET, respectively). Our present finding is in line with these results and provides further evidence to support that community-wide implementation of CT screening can contribute to the reduction of lung cancer mortality in the community.

In the present observation among residents of Hitachi City, a significant reduction of lung cancer mortality was observed during 2005–2009, which corresponds to 4–8 years after introduction of chest CT screening in both facilities. The timing of reduction in lung cancer mortality observed in the present study agrees well with that in the New York State cohort [9], in which the two rounds of screening provided a mortality reduction starting in the 6th–8th year after enrollment.

It remains unclear whether chest CT screening for lung cancer can decrease mortality among nonsmokers. However, given that more than a half of participants in CT screening for lung cancer at the two facilities in Hitachi City were nonsmokers and that 60% of lung cancer patients detected on that screening (as of March 2006) were nonsmokers, it may be reasonable to infer that observed reduction in lung cancer mortality among Hitachi residents may be due, at least in part, to the effect of CT screening on lung cancer mortality among nonsmokers. In fact, we also observed a significant reduction in lung cancer mortality for women, majority of whom are never smokers, during the third period (2005–2009), suggesting that CT screening is also effective in preventing lung cancer death among nonsmokers. Moreover, data from an ongoing cohort study of CT-screening participants including nonsmokers in Japan showed a reduction in lung cancer mortality [10]. The ACCP and ASCO guideline stated, based on available evidence, that CT screening for lung cancer should not be performed for low risk individuals [2]. However, given that nearly one-fourth of lung cancer in the world are unrelated to smoking [11] and in Japan, 31% and 80% of lung cancer deaths for men and women, respectively, are probably not related to smoking [12], the effectiveness of CT screening for lung cancer among nonsmokers should be evaluated in future studies.

The limitations of the present study warrant mention. The present analysis based on community level data, compared with cohort or randomized control studies, is more likely to suffer from bias. As a major concern, decreasing trend in lung cancer mortality observed in this population might be ascribed to factors other than chest CT screening. Of such factors, smoking is potentially important. Although long-term, representative data are not available on smoking prevalence in Hitachi, recent statistics on health indicators showed no material difference in smoking prevalence between Hitachi City and Ibaraki Prefecture [13]. In addition, no reduction

Table 3
Standardized mortality ratio[a] and its 95% confidence interval by sex, age, and period.

Age (year)	Men			Women		
	1995–1999	2000–2004	2005–2009	1995–1999	2000–2004	2005–2009
Total (50–79)						
O/E	194/201.4	228/227.6	203/267.1	57/61.8	57/65.2	53/71.3
SMR	0.96 (0.83, 1.11)	1.00 (0.88, 1.14)	0.76 (0.66, 0.87)	0.92 (0.70, 1.19)	0.87 (0.66, 1.13)	0.74 (0.56, 0.97)
50–59						
O/E	24/28.9	31/28.5	29/29.1	11/10.7	9/11	10/10.2
SMR	0.83 (0.53, 1.23)	1.09 (0.74, 1.54)	1.00 (0.67, 1.43)	1.03 (0.52, 1.85)	0.82 (0.38, 1.56)	0.98 (0.47, 1.81)
60–69						
O/E	75/76.2	80/82.5	61/89.2	18/18.2	19/21.1	18/24.0
SMR	0.98 (0.77, 1.23)	0.97 (0.77, 1.21)	0.68 (0.52, 0.88)	0.99 (0.59, 1.56)	0.90 (0.54, 1.40)	0.75 (0.45, 1.19)
70–79						
O/E	95/96.3	117/116.6	113/148.8	28/33	29/33.1	25/37.2
SMR	0.99 (0.80, 1.21)	1.00 (0.83, 1.20)	0.76 (0.63, 0.91)	0.85 (0.56, 1.23)	0.88 (0.59, 1.26)	0.67 (0.44, 0.99)

O, observed number of death; E, expected number of death; SMR, standardized mortality ratio.
[a] The expected number of lung cancer death was estimated using mortality data for whole population of Japan.

in SMR for cardiac disease, another smoking related disease, was observed during 2005–2009 in Hitachi (1.15 and 1.11 for men and women, respectively [13]). These data argue against smoking cessation as a plausible explanation for the reduction of lung cancer mortality observed among Hitachi residents. An increase of the incidence of lung cancer after the implementation of CT screening in the two medical facilities in Hitachi provides an additional support for the specific effect of CT screening, rather than other factors, in decreasing lung cancer mortality. Finally, we are uncertain whether the present finding in Hitachi could be generalized to other communities in Japan or other countries, which have different background in terms of risk factors for lung cancer as well as availability of medical service for patients with lung cancer detected on the screening.

5. Conclusion

In Hitachi City, a significant reduction in lung cancer mortality was observed 4–8 years after introduction of low-dose CT screening for lung cancer, suggesting that wide implementation of CT screening can decrease lung cancer mortality at community level. To enhance the benefit of CT screening and minimize its harm, future studies should be designed to address issues including clinical work-up of in-determined nodules, cost-effectiveness, and integration of smoking cessation practices [14].

Conflicts of interest

There are no conflicts of interest to disclose.

Acknowledgments

This study was supported by a Grant-in-Aid from the Ibaraki Prefecture for Clinical Cancer Research, 2010.

We thank Drs Hiromichi Aoki, Shimao Fukai, Masataka Irokawa, Yoshimichi Kawasaki, Kazuhide Kosaka, Masashi Kuramochi, Satoshi Morikawa, Kasuo Motegi, Kazuyoshi Nakahiro, Masayuki Nakayama, Yoshikatsu Nemoto, Hiroo Okazaki, Youichi Sugawara, Hiroyuki Takahashi, and Hajime Nakata and also all related staff who contributed to this screening program. We thank Ms Yuho Mizoue for help in manuscript preparation.

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Lung Cancer 75 (2012) 197–202

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Long-term prognosis of patients with lung cancer detected on low-dose chest computed tomography screening

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ARTICLE INFO

Article history:
Received 4 March 2011
Received in revised form 28 June 2011
Accepted 9 July 2011

Keywords:
Computed tomography
Chest
Japanese
Lung cancer
Prognosis
Screening

ABSTRACT

The effectiveness of lung cancer screening using low-dose chest computed tomography (CT) remains elusive. The present study examined the prognosis of patients with lung cancer detected on CT screening in Japanese men and women. Subjects were 210 patients with primary lung cancer identified on CT screening at two medical facilities in Hitachi, Japan, where a total of 61,914 CT screenings were performed among 25,385 screenees between 1998 and 2006. Prognostic status of these patients was sought by examining medical records at local hospitals, supplemented by vital status information from local government. The 5-year survival rate was estimated according to the characteristics of patients and lung nodule. A total of 203 (97%) patients underwent surgery. During a 5.7-year mean follow-up period, 19 patients died from lung cancer and 6 died from other causes. The estimated 5-year survival rate for all patients and for those on stage IA was 90% and 97%, respectively. Besides cancer stage, smoking and nodule appearance were independent predictors of a poor survival; multivariable-adjusted hazard ratio (95% confidence interval) was 4.7 (1.3, 16.5) for current and past smokers versus nonsmokers and 4.6 (1.6, 13.9) for solid nodule versus others. Even patients with solid shadow had a 5-year survival of 82% if the lesion was 20 mm or less in size. Results suggest that lung cancers detected on CT screening are mostly curative. The impact of CT screening on mortality at community level needs to be clarified by monitoring lung cancer deaths.

1. Introduction

Much attention has been paid to the effectiveness of low-dose chest computed tomography (CT) screening for lung cancer [1,2], which has poor prognosis. Screening with chest CT has been shown to have higher detection rate of lung cancer and, of cases identified, have higher curative resection rate than does screening with conventional chest X-ray [1–3]. However, data for the prognosis of lung cancer cases identified on CT screening are limited [4–6] and the effect of this screening procedure on mortality remains inconclusive. While several randomized controlled trials are ongoing [7–10], results of previous analyses [11–13] have not supported an effect of CT-based screening in lowering lung cancer mortality. Recently, however, the National Lung Screening Trial (NLST), a randomized trial targeted for current and former heavy smokers, found a 20% reduction in lung cancer death among participants screened with low-dose helical CT compared to participants screened with chest X-ray [14]. So far, screening lung cancer using CT has not been recommended in any set of guidelines except for research purpose [15,16].

In Hitachi Medical Area, a large-scale chest CT screening program for lung cancer has been introduced in two medical facilities since 1998 and 2001, respectively. We previously reported the characteristics of cancers detected on the CT screening [3,17]. In the present study, we followed 210 patients with lung cancer detected on the CT screening in collaboration with local hospitals and administrative office. The objectives of the present study were: (1) to estimate survival of prognosis of patients with lung cancer detected on CT screening and (2) to examine the prognosis of lung cancer patients according to a history of CT screening, patient characteristics, and the size and density of lung shadow on CT.

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doi:10.1016/j.lungcan.2011.07.002