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OBSERVED IN AUTOPSY CASES IN THE LIFE SPAN STUDY SAMPLE,
HIROSHIMA AND NAGASAKI, 1961-74

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原爆放射線との関連, 1961 - 74 年

TSUTOMU YAMAMOTO, M.D. 山本 務
YUKIKO SHIMIZU, B.S. 清水由紀子



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広島・長崎の寿命調査対象群における胃癌剖検例と原爆放射線との関連, 1961-74年

TSUTOMU YAMAMOTO, M.D. (山本 務)¹; YUKIKO SHIMIZU, B.S. (清水由紀子)²*Departments of Pathology¹ and Epidemiology & Statistics²*病理部¹ および疫学統計部²

SUMMARY

A study was made of the relation to atomic bomb radiation of 535 cases of gastric carcinoma among 4,694 deaths occurring in a fixed population of Hiroshima and Nagasaki who were autopsied between 1961 and 1974. The proportion of all autopsies with gastric carcinoma as autopsy diagnosis tended to be high in the high dose group, but it could not be concluded with the present amount of information that there is a relation between gastric carcinoma and radiation in this autopsy study. Although no specific distribution of the histological types of gastric carcinoma was noted by radiation dose, the data indicated increases in the degree of extension of tumor cells in the gastric wall and the degree of metastasis to the lymph nodes seemed to be high in the high dose group.

INTRODUCTION

It is well known that radiation has carcinogenic effects, and increased frequencies have been demonstrated in the A-bomb survivors of Hiroshima and Nagasaki for such malignancies as leukemia, thyroid cancer, lung cancer, breast cancer, and salivary gland tumor.¹⁻⁵ The question of the involvement of A-bomb radiation in the development of gastric carcinoma in the survivors is of great significance because of its high prevalence in the Japanese. A study of gastric carcinoma in A-bomb survivors was made earlier by Murphy and Yasuda.⁶ Yamamoto et al.,⁷ and Yamamoto and Kato⁸ studied the relation to A-bomb radiation of gastric carcinoma

要 約

1961-74年までの広島・長崎の固定人口集団内の剖検例 4,694例中にみられた胃癌 535例について原爆放射線との関係を追求した。全剖検例に対する胃癌の割合は高線量群に高い傾向を示すが、これだけの資料では胃癌と放射線との関連を結論づけることはできなかった。放射線量別に胃癌の組織型別の特異な分布は認められなかったが、癌細胞の胃壁内への深達度と、リンパ節への転移は高線量群に高い傾向が認められた。

緒 言

放射線が発癌作用をもっていることはよく知られていることであり、広島・長崎の原爆被爆者ではすでに白血病、甲状腺癌、肺癌、乳癌、唾液腺腫瘍などの発生率の増加が明らかにされている。¹⁻⁵ 原爆被爆者の胃癌の発生に原爆放射線が関与しているか否かは、日本人に胃癌の有病率が高いがゆえに大きな意味をもつものである。原爆被爆者における胃癌については、さきに Murphy と安田⁶の研究がある。また、山本ら⁷ならびに山本と加藤⁸は1961-68年の広島・長崎における胃癌剖検例について原爆放射線

cases autopsied in Hiroshima and Nagasaki between 1961 and 1968, but found no definite relation between gastric carcinoma and A-bomb radiation, neither in the proportion of all autopsies with this malignancy as autopsy diagnosis nor in histological characteristics.

Recently, Beebe et al.⁹ reported a relation between gastric carcinoma mortality and A-bomb radiation in a study based on death certificates for Hiroshima and Nagasaki. However, the autopsy confirmation rate for death certificate diagnoses of gastric carcinoma occurring in a fixed population of Hiroshima and Nagasaki was 83.9%,¹⁰ a discrepancy of 16.1% in the death certificate diagnoses.

To ascertain whether there is any relation to A-bomb radiation of gastric carcinoma observed at autopsy, the cases that were seen in a fixed population of Hiroshima and Nagasaki between 1961 and 1974 were reviewed in addition to those reported previously.

SAMPLE AND METHOD

In 1960, to study the late effects of the atomic bombs, ABCC (now RERF) in collaboration with JNII established the fixed population Life Span Study (LSS) sample of some 100,000 members in Hiroshima and Nagasaki. This sample, on which many reports have been made, is a specially selected fixed population of A-bomb survivors and their controls.¹¹ The LSS sample autopsy cases constitute a part or subgroup of all deaths occurring in that sample. Autopsies at Hiroshima and Nagasaki ABCC-JNII between 1961 and 1974 numbered 4,694, of which 535 were gastric carcinoma (Hiroshima 442 and Nagasaki 93) — an increase of 209 cases since the previous report.⁷ Cases with gastric carcinoma as the principal pathological diagnosis or as contributory or accessory diagnosis were used in this study, but excluded were post-gastrectomy cases which preclude histological confirmation even though they were diagnosed as gastric carcinoma clinically.

A study was made of the relationship of radiation dose to the proportion of gastric carcinoma autopsy cases to all autopsy cases; histological types of gastric carcinoma; degree of extension of the tumor in the various layers of the gastric wall (mucosal layer, submucosal layer, muscular layer, subserosal layer, serosal layer); metastasis

との関係をみたが、全剖検例に対する胃癌の割合、組織学的特徴などいずれにおいても胃癌と原爆放射線との間に明らかな関係を見ることができなかった。

最近、Beebe ら⁹は広島・長崎の死亡診断書による調査から、胃癌死亡率と原爆放射線との間に関係があることを述べている。しかし、広島・長崎の固定人口集団において死亡診断書の診断が胃癌であったものの剖検による確診率は83.9%¹⁰で、死亡診断書の診断との間に16.1%の差異がある。

胃癌剖検例についても原爆放射線との関係があるのではないかと確認するために、前回報告した症例をも含めて、1961—74年までの広島・長崎の固定人口集団内の胃癌剖検例について再検討した。

研究対象および方法

1960年、原爆による後障害を研究するために、ABCC（現在は放射線影響研究所）では、国立予防衛生研究所と共同で約10万名の固定人口集団である寿命調査対象群を広島・長崎に設定した。この集団についてはすでに多く述べられているが、これは特別に抽出された原爆被爆者と対照者の固定人口集団である。¹¹ この対象について行われた剖検例は寿命調査対象群の死亡者の一部で、寿命調査対象群における死亡例の副次群である。1961—74年まで広島・長崎 ABCC 一予研で行われた剖検例は4,694例であり、そのうち胃癌例は535例（広島442例、長崎93例）で前回報告時⁷より209例増加している。主要病理診断あるいは副次診断が胃癌例として診断されたものは症例として採用したが、胃摘出術後の症例で、胃癌の存在を組織学的に確認できなかった例はたとえ臨床診断が胃癌でも除外した。

胃癌剖検例の全剖検例に対する割合、胃癌組織分類、胃癌の胃壁各層（粘膜層、粘膜下層、筋肉層、漿膜下層、漿膜層）におよぶ深達度、各臓器およびリンパ節への癌転移、癌細胞の機能的表現としての粘液産生

TABLE 1 AUTOPSY RATE FOR ALL CAUSES AND FOR DEATH FROM GASTRIC CARCINOMA REPORTED ON DEATH CERTIFICATE AS UNDERLYING CAUSES BY RADIATION DOSE

表 1. 総剖検率と死亡診断書に記載されている原死因が胃癌であったものの剖検率, 線量別

	Radiation Dose in rad						NIC	Unk.
	Total	0	1-99	100-199	200-299	300+		
Autopsy rate for all causes (%)	31.7	30.1	35.2	38.9	42.4	43.4	27.1	36.0
Deaths autopsied for all causes	4694	148 ^c	1788	155	75	92	1028	71
Autopsy rate for gastric carcinoma (%)	36.3	34.3	38.7	42.9	42.9	29.2	36.0	34.2
Deaths autopsied for gastric carcinoma	429	141	142	12	6	7	116	5

NIC: Not-in-city at the time of the A-bomb

原爆時市内にいなかったもの

Unk.: Unknown

不明

of the tumor to various organs and lymph nodes; mucus production as a functional expression of cancer cells, etc. Because there is no histological classification of gastric carcinoma that is common to all countries of the world, the authors have based theirs on the classification of Oota¹² which is representative in Japan, and on the simple classification criteria of Lauren.¹³ The degree of mucus production was classified into four grades, ranging from high production with evidence of mucus retention to production of an extent that no mucus producing cells (signet-ring cells) could be observed.

For the frequency of diseases found in the autopsy cases to be regarded as estimates of the frequency in the LSS sample, there should be no bias of the autopsy cases from deaths occurring in that sample with regard to all factors including sex, age, exposure dose, and disease. The absence of such biases becomes especially important when the autopsy rate is low. When the proportion of gastric carcinoma deaths that are autopsied, by radiation dose, is relatively the same as the proportion of all autopsied deaths by dose, there is presumed to be no bias by radiation dose.

Table 1 shows by radiation dose for the period 1961-74 the autopsy rates for all causes in the LSS sample and the autopsy rates for gastric carcinoma given as the underlying cause of death in death certificates. The autopsy rates for all causes increased with dose, however, those for gastric carcinoma showed a different tendency with the same rates in both the 0-99

度などに対する放射線量との関連を検討した。胃癌の組織分類は世界各国に共通の分類がないので日本で代表的な太田による分類,¹² および簡単な Lauren の分類基準¹³ に基づいた。粘液産生度の分類は粘液産生が高度で、粘液貯留の認められるものから、粘液産生細胞(印環細胞)の認められない程度のものまでを四段階に分けた。

剖検例に認められる疾患の頻度を観察する場合、それを寿命調査対象群における頻度とみなすためには、剖検には、性、年齢、被曝線量、疾病などあらゆる要素について寿命調査対象群の死亡者からの偏りがあってはならない。剖検率が低い場合には、これらの偏りのないことが特に重要となってくる。いまここに線量別の胃癌剖検例の割合が、全剖検例の線量別割合に比例している場合、線量による偏りは無いと考えられる。

表 1 に 1961 年より 1974 年までの寿命調査対象群における総剖検率と、死亡診断書に記載されている原死因が胃癌であったものの剖検率を被曝線量別に示した。総剖検率は線量と共に増加しているのに反し、胃癌剖検率は同様の傾向を示さず、0-99 rad 群と

and 100+ rad dose groups. Whereas the autopsy rates for all causes are not equal by radiation dose, these rates for gastric carcinoma are not in proportion to those for all causes. Therefore, it can be considered that in the gastric carcinoma autopsy cases there is a bias between the dose groups related to disease.

The true relation of gastric carcinoma to radiation cannot be seen in this case merely by making a dose-specific study of the crude proportion of all autopsies with gastric carcinoma as autopsy diagnosis. Thus, in the present study, a "corrected" proportion of gastric carcinoma was also calculated by the following formula to counteract this bias:

$$\frac{a \times \frac{\frac{D_1}{D}}{\frac{A_1}{A}} + b \times \frac{\frac{D_2}{D}}{\frac{A_2}{A}}}{A}$$

a: number of cases that were gastric carcinoma both by autopsy and by death certificate

b: number of gastric carcinoma cases detected for the first time by autopsy

D₁: number of deaths derived from death certificates with gastric carcinoma given as the cause of death

D₂: number of deaths derived from death certificates with other than gastric carcinoma given as the cause of death

D: D₁ + D₂

A₁: number of autopsy cases with gastric carcinoma given as cause of death in the death certificate

A₂: number of autopsy cases with gastric carcinoma not given as cause of death in the death certificate

A: A₁ + A₂

100 rad 以上群は共に同率である。総剖検率は線量別に一様でないが、胃癌剖検率は総剖検率に比例していない。このため、胃癌剖検例には線量群間に疾病による偏りがあると目される。

この場合、単に胃癌剖検例の全部剖検例に対する粗割合を被曝線量別に観察するだけでは、真の胃癌と放射線との関係を見ることができない。そこで、本研究ではこの偏りを是正する一方法として、下記の数式を用い訂正胃癌有病割合を算出した。

a: 剖検でも死亡診断書でも胃癌であった例数

b: 剖検により初めて見いだされた胃癌例

D₁: 死亡診断書の胃癌例

D₂: 死亡診断書中の胃癌以外の死亡数

D: D₁ + D₂

A₁: 死亡診断書が胃癌であったものの剖検数

A₂: 死亡診断書が胃癌でなかったものの剖検数

A: A₁ + A₂

For all autopsies (A) to be a random subgroup for diseases in all deaths (D), the proportion of

剖検総数(A)が死亡総数(D)の任意の疾患副次群で

D_1 (gastric carcinoma in death certificates) in D should be equal to the proportion of A_1 (autopsied gastric carcinoma in death certificates) in A .

$D_1/D / A_1/A$ is the correction term when A is not a random sample of D . When $D_1/D = A_1/A$, that is when A is a random subgroup of D , a "corrected proportion" is identical to the heretofore employed crude proportion $\frac{a+b}{b}$.

The T65D estimates in rad were used as the A-bomb radiation dose.¹⁴ Individual exposure doses have been calculated for almost the entire fixed population from the air dose, taking into consideration the various shielding configurations. Few gastric carcinoma cases were exposed to high doses and those with 200+ rad in particular numbered only 19 in Hiroshima and Nagasaki combined. Therefore, those exposed to 100+ rad were used as the high dose group in the analysis of the pathological findings (degree of tumor extension, metastasis, mucus production).

RESULTS

Proportion of All Autopsies with Gastric Carcinoma as Autopsy Diagnosis

The crude proportions of all autopsies with gastric carcinoma as autopsy diagnosis were studied by radiation dose and city for the 535 cases of gastric carcinoma (Table 2A, Figure 1). The 200-299 rad group of the two cities combined, the 200-299 rad group of Hiroshima, and the 300+ rad group of Nagasaki showed higher crude proportions than the 0 rad group, but without statistically significant difference. Compared with the relation between crude proportion of gastric carcinoma and radiation dose, a corrected proportion of gastric carcinoma had a marked tendency to be higher in the high dose group than in the low dose group (Table 2B). This tendency was remarkable especially in Nagasaki, where a statistically significant difference was noted in a corrected gastric carcinoma proportion between the 0 rad and the 200+ rad groups ($P < 0.05$). However, this finding might have occurred due to the small number of gastric carcinoma cases (6) in the latter group. A study by sex revealed the same finding.

The relative risks of gastric carcinoma in the 200+ rad versus 0 rad group were calculated by

あるためには、 D に対する D_1 (死亡診断書の胃癌例)の割合が、 A に対する A_1 (死亡診断書中の胃癌剖検数)の割合に一致しなければならない。

$D_1/D / A_1/A$ は A が D の任意の副次群でない場合の訂正数値である。 $D_1/D = A_1/A$ の場合、すなわち A が D の任意の副次群である場合は、その訂正の割合は従来使われた粗の割合 $\frac{a+b}{b}$ に一致する。

原爆放射線量としてT65D (rad単位暫定推定線量)を使用した。¹⁴ この空気線量から、種々の遮蔽物を考慮に入れた個々の被曝線量が、固定人口集団のほぼ全員について計算されている。高線量被曝胃癌例、特に200 rad以上の被曝例は広島・長崎両市で19例と少数のため、病理学的所見(癌深達度、転移、粘液産生度)の解析には100 rad以上を高線量群として使用した。

結 果

被爆者剖検例の胃癌有病割合

535例の剖検胃癌例について被曝線量別、都市別に粗胃癌有病割合を検討した(表2A, 図1)。両市合計で200-299 rad群、広島は200-299 rad群、長崎では300 rad以上の群は0 rad群に比して高い粗胃癌有病割合を示している。しかし統計的には有意差を認めない。粗胃癌有病割合と放射線量との関係に比して、訂正胃癌有病割合は低線量群より高線量群に高い傾向が強みられる(表2B)。特に長崎においてその傾向が顕著であり、0 rad群と200 rad以上群の訂正胃癌有病割合は統計的有意差を認めた($P < 0.05$)。しかしこの所見は後者の胃癌例が少数(6例)であったために生じたものかも知れない。また、男女別に検討したが同様の所見であった。

0 rad胃癌有病割合に対する200 rad以上被爆者の

FIGURE 1 PROPORTION OF GASTRIC CARCINOMA AMONG ALL AUTOPSIES BY RADIATION DOSE & CITY

図1 全剖検例中における胃癌例の割合、線量および都市別

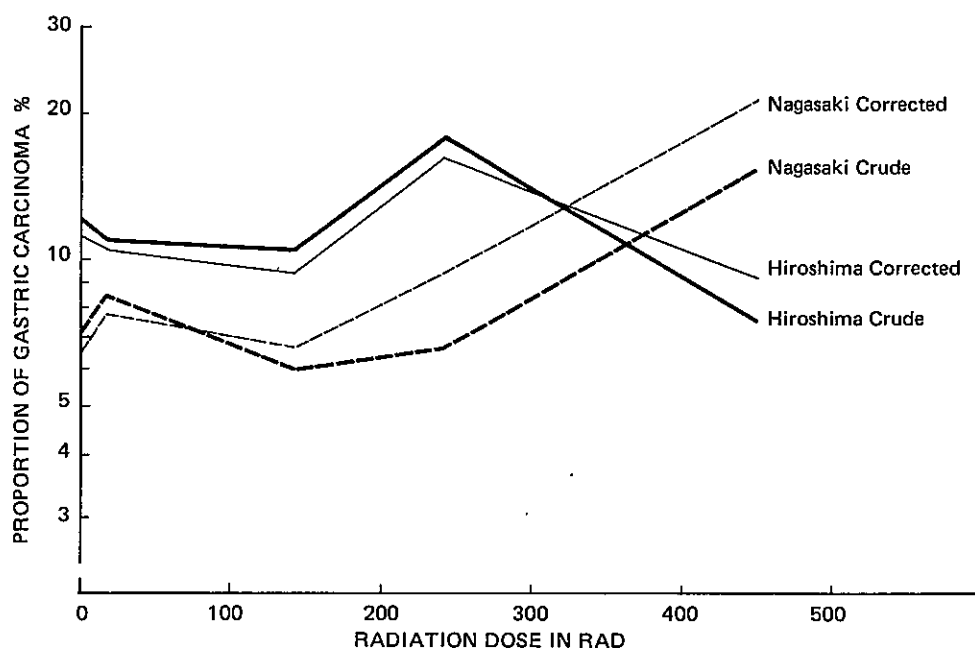


TABLE 2 PROPORTION OF ALL AUTOPSIES WITH GASTRIC CARCINOMA FOUND AT AUTOPSY & CORRECTED PROPORTION OF GASTRIC CARCINOMA BY RADIATION DOSE & CITY

表2 剖検で認められた胃癌例の全剖検例に対する割合および訂正胃癌有病割合、線量および都市別

	Radiation Dose (rad)								
	Total	0	1-99	100-199	200-299	300 +	200 +	NIC	Unk.
A. Proportion of All Autopsies with Gastric Carcinoma									
Total	11.4 (535)	11.6 (172)	10.5 (187)	9.1 (14)	13.5 (10)	9.8 (9)	11.4 (19)	13.2 (136)	9.8 (7)
Hiroshima	12.0 (442)	12.1 (159)	11.2 (146)	10.5 (11)	18.1 (8)	7.6 (5)	11.8 (13)	13.3 (110)	7.2 (3)
Nagasaki	9.3 (93)	7.3 (13)	8.5 (41)	6.1 (3)	6.7 (2)	14.7 (4)	10.7 (6)	12.7 (26)	13.0 (4)
B. Corrected Proportion									
Total	10.5	10.6	9.9	8.4	13.3	12.3	12.8	11.0	10.3
Hiroshima	11.1	11.2	10.7	9.5	16.4	9.3	12.2	11.5	7.5
Nagasaki	8.3	6.5	7.8	6.7	9.6	21.3	15.2	9.0	14.2

(): Gastric carcinoma found on autopsy.

剖検で認められた胃癌例数

TABLE 3 RELATIVE RISK (200+ rad / 0 rad) & RELATIVE RISK BASED ON CORRECTED PROPORTION OF GASTRIC CARCINOMA BY AGE ATB & PERIOD

表3 胃癌の相対危険度(200 rad 以上 / 0 rad) および訂正有病割合に基づく、胃癌の相対危険度、原爆時年齢および期間別

Age ATB	Period			
	Total	1961-64	1965-68	1969-74
A. Relative Risk				
Total	0.98 (19)	1.4 (6)	0.80 (6)	0.90 (7)
<40	0.83 (6)	0.0 (0)	0.66 (2)	1.2 (4)
40-49	0.55 (3)	1.1 (2)	0.48 (1)	0.0 (0)
50+	1.4 (10)	2.5 (4)	1.2 (3)	0.99 (3)
B. Relative Risk based on Corrected Proportion				
Total	1.2	1.9	0.90	1.1
<40	1.2	0.0	1.1	1.3
40-49	0.73	1.4	0.43	0.0
50+	1.6	2.4	1.3	0.96

(): Gastric carcinoma in 200+ rad group.

age at time of bomb (ATB) and period of death, based on crude and corrected proportions (Table 3). Although the relative risk based on corrected proportion showed higher values than that based on crude proportion, they showed similar tendencies as to changes by age ATB and period of death. By age ATB, the relative risk was the highest in the 50+ group and the lowest in the 40-49 group. By period of death, the relative risk was the highest in the 1961-64 group. The relative risk was high in the period 1969-74 in the less than 40 group ATB and it was high in the period 1961-64 in the 40-49 group and the 50+ group. Suggestive findings were obtained for the 50+ group in statistical tests of a corrected proportion in a comparison between the 0 rad group and the 200+ rad group. However, for the period 1961-64 no statistically significant difference was noted in the proportion of gastric carcinoma between the 0 rad and the 200+ rad groups.

Histological Classification of Gastric Carcinoma

A study of the distribution by radiation dose of the histologic types of gastric carcinoma as classified by Oota's criteria revealed a tendency for the tubular medullary type, scirrhous type, and muconodular type to occur more frequently in the high dose group than in the low dose group, but no statistically significant difference

胃癌有病割合の相対危険度を被爆時年齢別、死亡期間別に、粗胃癌有病割合、訂正胃癌有病割合に基づいて算出した(表3)。訂正胃癌有病割合を基にした相対危険度は粗胃癌有病割合を基にした相対危険度よりも高い値を示すが、被爆時年齢別、死亡期間別による相対危険度の変化は同様の傾向を示した。すなわち、被爆時年齢別では50歳以上群が最も高く、40-49歳群は最も低い。死亡時期別では1961-64年群に最も高い相対危険度を示す。また、被爆時年齢40歳以下の群では1969年-74年が高く、40-49歳群、50歳以上群では、1961-64年に相対危険度が高かった。50歳以上の群では訂正胃癌有病割合における0 rad 群と200 rad 以上群との統計的検定において示唆的所見を得ている。しかし1961-64年群では0 rad と200 rad 以上群では胃癌有病割合に統計的有意差は認めなかった。

胃癌の組織型分類

胃癌の組織型分類(太田)を行い、その分布を被曝線量別にみると、髄様腺管型、硬癌型、粘液細胞型が低線量群に比較して高線量群に多い傾向を示したが、

TABLE 4 DISTRIBUTION OF GASTRIC CARCINOMA BY HISTOLOGIC TYPE & RADIATION DOSE

表4 胃癌の組織型分類, 線量別

A. Histologic type Oota¹²

Radiation Dose (rad)	Total	Papillary tubular	Tubular medullary	Acinous	Scirrhou	Muco-cellular	Muco-nodular	Adeno-acanthoma	Other
Total No.	535	48	157	23	132	39	35	9	92
%	100.0	9.0	29.3	4.3	24.7	7.3	6.5	1.7	17.2
0 No.	172	13	49	10	30	15	13	4	38
%	100.0	7.6	28.5	5.8	17.4	8.7	7.6	2.3	22.1
1-99 No.	187	26	55	6	48	15	6	4	27
%	100.0	13.9	29.4	3.2	25.7	8.0	3.2	2.1	14.4
100-199 No.	14	1	7	1	2	—	1	—	2
%	100.0	7.1	50.0	7.1	14.3	—	7.1	—	14.3
200+ No.	19	1	6	—	5	1	3	—	3
%	100.0	5.3	31.6	—	26.3	5.3	15.8	—	15.8
NIC No.	136	7	40	4	44	8	11	1	21
%	100.0	5.1	29.4	2.9	32.4	5.9	8.1	0.7	15.4
Unk. No.	7	—	—	2	3	—	1	—	1
%	100.0	—	—	28.6	42.9	—	14.3	—	14.3

B. Histologic type Lauren¹³

Radiation Dose (rad)	Total	Intestinal	Diffuse	Mixed	Other
Total	No. 535	221	211	19	84
	% 100.0	41.3	39.4	3.6	15.7
0	No. 172	68	61	8	35
	% 100.0	39.5	35.5	4.7	20.3
1-99	No. 187	82	75	6	24
	% 100.0	43.9	40.1	3.2	12.8
100-199	No. 14	6	4	2	2
	% 100.0	42.9	28.6	14.3	14.3
200+	No. 19	7	9	—	3
	% 100.0	36.8	47.4	—	15.8
NIC	No. 136	56	58	3	19
	% 100.0	41.2	42.6	2.2	14.0
Unknown	No. 7	2	4	—	1
	% 100.0	28.6	57.1	—	14.3

was found (Table 4A). A similar study of distribution by dose using Lauren's classification showed no difference in the distribution of the intestinal type and the diffuse type (Table 4B). From simply a morphological point of view, the tubular medullary type and scirrhou type by Oota's classification generally equate with the intestinal type and diffuse type by Lauren's classification.

Degree of Extension of Gastric Carcinoma

The degree of extension of gastric carcinoma was studied by radiation dose and histological type using Oota's classification (Table 5).

統計的な有意性を得なかった(表4A)。また, Lauren の分類により同様の線量別分布をみると, 放射線量 による腸管型と瀰漫型との分布の差は認められない (表4B)。単に形態学的観点よりすれば, 太田の 髄様腺管型, 硬癌型はそれぞれ Lauren の腸管型, 瀰漫型にほぼ相当する。

胃癌の深達度

胃癌の深達度を放射線量別, 太田の分類による組織

TABLE 5 EXTENSION BY RADIATION DOSE AND HISTOLOGIC TYPE

表 5 癌の深達度，線量および組織型別

Histologic Type	Radiation Dose in rad		Degree of Extension			
			Total	Restriction in Gastric Wall	Lymph Channel	Blood Vessel
Total	Total	No.	446	46	238	162
		%	100.0	10.3	53.4	36.2
	0	No.	134	16	75	43
		%	100.0	11.9	56.0	32.1
	1-99	No.	162	21	85	56
		%	100.0	13.0	52.5	34.6
	100+	No.	28	—	17	11
		%	100.0	—	60.7	39.3
	NIC	No.	116	9	56	51
		%	100.0	7.8	48.3	44.0
	Unk.	No.	6	—	5	1
		%	100.0	—	83.3	16.7
Tubular medullary	Total	No.	157	28	81	48
		%	100.0	17.8	51.6	30.6
	0	No.	49	10	27	12
		%	100.0	20.4	55.1	24.5
	1-99	No.	55	13	26	16
		%	100.0	23.6	47.3	29.1
	100+	No.	13	—	9	4
		%	100.0	—	69.2	30.8
	NIC	No.	40	5	19	16
		%	100.0	12.5	47.5	40.0
	Unk.	No.	—	—	—	—
		%	—	—	—	—
Scirrhou	Total	No.	132	2	82	48
		%	100.0	1.5	62.1	36.4
	0	No.	30	—	20	10
		%	100.0	—	66.7	33.3
	1-99	No.	48	2	31	15
		%	100.0	4.2	64.6	31.3
	100+	No.	7	—	4	3
		%	100.0	—	57.1	42.9
	NIC	No.	44	—	24	20
		%	100.0	—	54.5	45.5
	Unk.	No.	3	—	3	—
		%	100.0	—	100.0	—

Whereas extension was noted to have been restricted to one of the layers of the gastric wall in 11.9% of the cases in the 0 rad group, it was found to have extended to all layers of the gastric wall in all cases in the 100+ rad group. This tendency was seen in all cases of gastric carcinoma and in the cases of tubular medullary type. This difference in the degree of extension between the 0 rad group and the 100+ rad group is statistically significant. The scirrhou

型別にみた(表5). 0 rad 群では胃壁内のいずれかの層に留まっているものが11.9%みられるのに対して, 100 rad 以上の群では全例が全胃壁層に深達している. この傾向は全胃癌例においても, また髄様腺管型のものにもみられる. この 0 rad 群と 100 rad 群との癌深達度の差は統計的に有意である. 硬癌型では 0 rad 群を含む全例に全胃壁層への浸潤が認め

TABLE 6 DISTRIBUTION OF THE NUMBER OF METASTASIS SITE TO LYMPH NODE
BY RADIATION DOSE AND HISTOLOGIC TYPE

表 6 癌転移のあったリンパ節の部位数の分布、線量および組織型別

Histologic Type	Radiation Dose in rad		Number of Metastasis Site				
			Total	0	1-2	3+	1+*
Total	Total	No.	535	132	276	127	403
		%	100.0	24.7	51.6	23.7	75.3
	0	No.	172	43	88	41	129
		%	100.0	25.0	51.2	23.8	75.0
	1-99	No.	187	50	99	38	137
		%	100.0	26.7	52.9	20.3	73.3
	100+	No.	33	8	12	13	25
		%	100.0	24.2	36.4	39.4	75.8
	NIC	No.	136	29	73	34	107
		%	100.0	21.3	53.7	25.0	78.7
Tubular medullary	Unk.	No.	7	2	4	1	5
		%	100.0	28.6	57.1	14.3	71.4
	Total	No.	157	45	75	37	112
		%	100.0	28.7	47.8	23.6	71.3
	0	No.	49	14	23	12	35
		%	100.0	28.6	46.9	24.5	71.4
	1-99	No.	55	20	25	10	35
		%	100.0	36.4	45.5	18.2	63.6
	100+	No.	13	2	4	7	11
		%	100.0	15.4	30.8	53.8	84.6
Scirrhou	NIC	No.	40	9	23	8	31
		%	100.0	22.5	57.5	20.0	77.5
	Unk.	No.	—	—	—	—	—
		%	—	—	—	—	—
	Total	No.	132	20	78	34	112
		%	100.0	15.2	59.1	25.8	84.8
	0	No.	30	4	19	7	26
		%	100.0	13.3	63.3	23.3	86.7
	1-99	No.	48	8	28	12	40
		%	100.0	16.7	58.3	25.0	83.3
Scirrhou	100+	No.	7	3	2	2	4
		%	100.0	42.9	28.6	28.6	57.1
	NIC	No.	44	4	28	12	40
		%	100.0	9.1	63.6	27.3	90.0
	Unk.	No.	3	1	1	1	2
		%	100.0	33.3	33.3	33.3	66.6

*Metastasis to more than one site. 1箇所以上の部位への転移

showed extension to all layers of the gastric wall in all cases even in the 0 rad group.

られる。

Metastasis of Gastric Carcinoma

The number of sites of lymph nodes with metastasis of the carcinoma was examined by radiation dose and histological type (Table 6). The proportion of the cases presenting metastasis to one or more sites among all gastric carcinoma cases was 75.0% in the 0 rad group, not different

胃癌の転移

被曝線量別、組織型別に癌転移のあったリンパ節の部位数をみた(表6)。1箇所以上の転移を示した例の割合は全胃癌例において0 rad群では75.0%、

TABLE 7 DISTRIBUTION OF THE NUMBER OF METASTASIS TO ORGAN
BY RADIATION DOSE AND HISTOLOGIC TYPE

表 7 臓器転移の分布、線量および組織型別

Histologic Type	Radiation Dose in rad		Number of Metastasis					
			Total	0	1-3	4-6	7+	1+*
Total	Total	No.	535	127	205	134	69	408
		%	100.0	23.7	38.3	25.1	12.9	76.3
	0	No.	172	39	67	47	19	133
		%	100.0	22.7	39.0	27.3	11.1	77.3
	1-99	No.	187	52	69	37	29	135
		%	100.0	27.8	36.9	19.8	15.5	72.2
	100+	No.	33	4	17	7	5	29
		%	100.0	12.1	51.5	21.2	15.2	87.9
	NIC	No.	136	30	50	40	16	106
		%	100.0	22.1	36.8	29.4	11.8	77.9
	Unk.	No.	7	2	2	3	—	5
		%	100.0	28.6	28.6	42.9	—	71.4
Tubular medullary	Total	No.	157	49	64	27	17	108
		%	100.0	31.2	40.8	17.2	10.8	68.8
	0	No.	49	14	21	8	6	35
		%	100.0	28.6	42.9	16.3	12.2	71.4
	1-99	No.	55	23	21	6	5	32
		%	100.0	41.8	38.2	10.9	9.1	58.2
	100+	No.	13	1	6	4	2	12
		%	100.0	7.7	46.2	30.8	15.4	92.3
	NIC	No.	40	11	16	9	4	29
		%	100.0	27.5	40.0	22.5	10.0	72.5
	Unk.	No.	—	—	—	—	—	—
		%	—	—	—	—	—	—
Scirrhou	Total	No.	132	17	44	48	23	115
		%	100.0	12.9	33.3	36.4	17.4	87.1
	0	No.	30	3	10	15	2	27
		%	100.0	10.0	33.3	50.0	6.7	90.0
	1-99	No.	48	6	17	14	11	42
		%	100.0	12.5	35.4	29.2	22.9	87.5
	100+	No.	7	1	3	1	2	6
		%	100.0	14.3	42.9	14.3	28.6	85.7
	NIC	No.	44	6	13	17	8	38
		%	100.0	13.6	29.5	38.6	18.2	86.4
	Unk.	No.	3	1	1	1	—	2
		%	100.0	33.3	33.3	33.3	—	66.7

*Metastasis to more than one organ. 1 箇所以上の臓器への転移

from that in the 100+ rad group with 75.8%. By histological type the proportions were 71.4% and 84.6% respectively for the tubular medullary type. Although the proportion was thus higher in the 100+ rad group, the difference was not statistically significant. The scirrhou type also showed no tendency for the proportion to be higher in the high dose group in a comparison between the 0 rad and the 100+ rad groups.

100 rad 以上群では75.8%と差はない。組織型別にみても髄様腺管型ではそれぞれ71.4%、84.6%と100 rad 以上群に高いが、統計的な有意差はなく、硬癌型でも0 rad 群と100 rad 以上群との間にも高線量群に多いという傾向はなかった。

TABLE 8 MUCUS PRODUCTION BY HISTOLOGIC TYPE (LAUREN) AND RADIATION DOSE

表 8 粘液産生度，組織型 (Lauren) および線量別

Radiation Dose in rad		Intestinal					Diffuse				
		Total	1*	2	3	4	Total	1*	2	3	4
Total	No.	221	24	15	63	119	211	19	90	70	32
	%	100.0	10.9	6.8	28.5	53.8	100.0	9.0	42.7	33.2	15.2
0	No.	68	12	4	20	32	61	5	33	17	6
	%	100.0	17.6	5.9	29.4	47.1	100.0	8.2	54.1	27.9	9.8
1-99	No.	82	2	8	21	51	75	7	30	28	10
	%	100.0	2.4	9.8	25.6	62.2	100.0	9.3	40.0	37.3	13.3
100+	No.	13	2	1	6	4	13	1	7	2	3
	%	100.0	15.4	7.7	46.2	30.8	100.0	7.7	53.8	15.4	23.1
NIC	No.	56	7	2	16	31	58	6	18	21	13
	%	100.0	12.5	3.6	28.6	55.4	100.0	10.3	31.0	36.2	22.4
Unk.	No.	2	1	—	—	1	4	—	2	2	—
	%	100.0	50.0	—	—	50.0	100.0	—	50.0	50.0	—

*1 — Mucus pools; 2 — Signet cells, many; 3 — Signet cells, few; 4 — Signet cells, none.

粘液プール

印環細胞多数

印環細胞少数

印環細胞なし

Examination by radiation dose of the distribution of cases with metastasis to lymph nodes of one or more showed that 68.2% presented metastasis to one or two sites and 31.8% to three or more sites in the 0 rad group, and that 48.0% presented metastasis to one or two sites and 52.0% to three or more sites in the 100+ rad group; there being more cases with metastasis to the lymph nodes of three or more sites in the 100+ rad group. This tendency was seen for both the tubular medullary type and the scirrhous type.

A similar examination by radiation dose and histological type of metastasis of gastric carcinoma to various organs revealed a high metastasis rate in the 100+ rad group, with metastasis to one or more sites in 77.3% of all gastric carcinoma cases in the 0 rad group and in 87.9% in the 100+ rad group (Table 7). This tendency was also noted for the tubular medullary type, but not for the scirrhous type, and the difference was not statistically significant. In the cases with metastasis to one or more organs, no difference was noted by radiation dose in the number of organs with metastasis.

Mucus Production of Gastric Carcinoma

The relation of radiation dose to mucus production was studied by histological type using Lauren's classification (Table 8). Cases of the intestinal type with no signet-ring cells accounted for 30.8% in the high dose group exposed to 100+ rad, lower than the 47.1% in

1 箇所以上のリンパ節に転移している例の分布を放射線量別にみると，0 rad 群では 1—2 箇所の転移が 68.2%，3 箇所以上 31.8%，100 rad 以上群では 1—2 箇所 48.0%，3 箇所以上 52.0% と 100 rad 以上群に 3 箇所以上のリンパ節転移を示す例が多かった。この傾向は髄様腺管型，硬癌型のいずれにもみられた。

同様に，被曝線量別，組織型別に各臓器への胃癌転移をみると，全胃癌例で一つの臓器以上に転移をみたのは 0 rad 群で 77.3%，100 rad 以上群では 87.9% で 100 rad 以上群に臓器転移率が高い (表 7)。この傾向は髄様腺管型にも認められたが，硬癌型には認められず，その差は統計的に有意性はなかった。

1 臓器以上転移している例で，転移臓器数に放射線量による差異は認められなかった。

胃癌の粘液産生度

Lauren 分類による組織型別に粘液産生度に対する放射線量の間接関係をみた (表 8)。腸管型では 100 rad 以上の高線量群で印環細胞のみられない例は 30.8%，0 rad 群の 47.1% に比して低い。瀰漫型では高線量

the 0 rad group. The diffuse type with no signet-ring cells accounted for 23.1% in the high dose group, higher than the 9.8% in the 0 rad group. Though similar tendencies were not evident for the intestinal type and the diffuse type, in neither case was a statistically significant difference found.

DISCUSSION

Recent studies based on death certificates have affirmed a relation between A-bomb radiation and gastric carcinoma.⁹ The data suggest that relatively large radiation doses might be required to clearly elevate the frequency of stomach carcinoma. Nakamura¹⁵ made a detailed analysis of the high dose range concerning death certificates in the LSS sample 1950-73, Hiroshima and Nagasaki. His report suggests that the "humped" dose response curve for the mortality rate from stomach carcinoma in Hiroshima, which peaked at 400-499 rad and then declined, may reflect true dose response obscured by artifacts related to the compilation of the radiation dose estimates. In Nagasaki, the effects of radiation on stomach cancer mortality were not clear. However, no definite relation could be seen between A-bomb radiation and gastric carcinoma in the present study of autopsy cases including the cases of the previous study, although findings of some relation to radiation were obtained for the proportion of gastric carcinoma, degree of extension and metastasis.

Regarding the difference between the results of the death certificate study and those based on autopsy cases, the following two points can be considered:

1) There is a limit to the reliability of the diagnosis of gastric carcinoma given in death certificates. For example, in this study the confirmation rate at autopsy for gastric carcinoma reported on death certificates was 83%, and 66.5% of the gastric carcinomas found at autopsy had been diagnosed as such on the death certificates. But study is possible on all cases of death occurring in the LSS sample.

2) Reliability of diagnosis is high in the study based on autopsy cases, but the autopsy study group is not representative of all deaths occurring in the study sample. The probability that a given death will result in autopsy

群で印環細胞の見られない例は23.1%で0 rad群の9.8%に比して高い。腸管型、瀰漫型に同じ傾向が認められないが、いずれにおいても統計的な有意性は認められない。

考 察

最近の死亡診断書による調査研究⁹では、原爆放射線と胃癌との関係が肯定されている。この資料は、胃癌の発生頻度に明白な上昇を認めるためには比較的高線量の放射線が必要であることを示唆している。中村¹⁵は広島・長崎の1950-73年の寿命調査対象者の死亡診断書をもとに、高線量域被爆者について詳細な解析を行った。その結果、広島の胃癌による死亡率の「こぶ型」の線量反応曲線は400-499 radをピークとして下降しているが、これは被曝線量の推定の際に人為的に不明確になった真の線量反応曲線を反映するかもしれないことを示唆している。長崎では放射線の胃癌死亡率への影響は明らかではなかった。剖検例の検討では前回の症例をも含めた今度の検討においても、胃癌有病割合、癌深達度、癌転移などにある程度放射線との関係を認められる所見が得られたが、明確に原爆放射線と胃癌との関係を見いだすことができなかった。

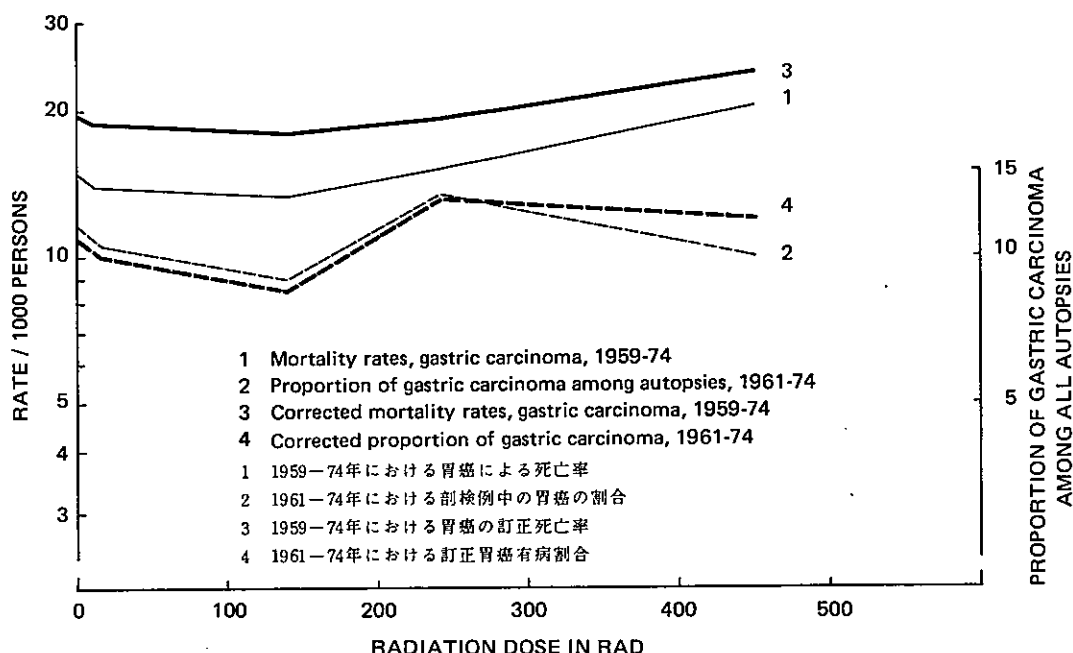
死亡診断書を用いた調査結果と剖検例による検討結果の相違については、その理由として次の2点が考えられる。

1) 死亡診断書による胃癌の診断には信頼性に限界がある。たとえば、本研究において、死亡診断書の診断が胃癌であったものの剖検による確診率は83%、剖検で胃癌が発見されたものの66.5%は死亡診断書の診断も同様であった。しかし、寿命調査対象群の全死亡者について検討が可能である。

2) 剖検例による検討は、診断の正確性は高いが、剖検調査群は必ずしも調査対象群の全死亡者を代表していない。死亡者の剖検を行う確率

FIGURE 2 MORTALITY FROM GASTRIC CARCINOMA — COMPARISON OF FOUR INDICES BY RADIATION DOSE

図2 胃癌による死亡率—四つの指標による比較、線量別



depends upon the diagnosis on the death certificate, the person's age, and the radiation dose received.

は死亡診断書の診断、その人の年齢および被曝線量に左右される。

From Table 1, it can be seen that the autopsy rate for cases with death certificate diagnoses of gastric carcinoma is the same for both the 0-99 rad and 100+ rad dose groups, whereas the autopsy rate for all causes in the higher dose group is 25% greater than the low dose group. This explains the lowered crude proportion of all autopsies with gastric carcinoma as autopsy diagnosis in the high dose group. Since neither the death certificate nor autopsy data are free from errors (the first suffers from confirmation and detection errors, the second from a selective bias), a "corrected" proportion which combines the information from both sources was used in the analysis of the present study, but the relation between radiation dose and the autopsy diagnosed cases of gastric carcinoma could not be clarified. Incidentally, the corrected mortality rate by gastric carcinoma based on death certificates with reference made also to the autopsy diagnosis, shows a relation to radiation dose and high rates at high doses (Figure 2).

表1から、死亡診断書が胃癌の剖検割合は0-99 rad 群および100 rad 以上群共に同じであるが、高線量群の総剖検率は低線量群より25%高いことがわかる。このことは高線量群の総剖検例の粗胃癌有病割合の低下を説明している。死亡診断書も剖検資料も誤りは免れることはできないので(前者は確認および発見の誤り、後者に選取上の偏りがある)、本調査の解析では両者の情報を合わせた訂正有病割合を用いたが、放射線量と胃癌剖検例との関係を明瞭にすることはできなかった。ちなみに剖検診断を加味した死亡診断書による訂正胃癌死亡率は放射線量と関連し、高線量に高い事を示している(図2)。

The numerical expression for the calculation of the corrected mortality rate for gastric carcinoma is:

$$\text{Corrected mortality rate: } \frac{D_1 \times \frac{a}{A_1} + D_2 \times \frac{b}{A_2}}{N}$$

N: total number of population

a, b, A₁, A₂, D₁, D₂ (see Sample and Method)

This rate shows higher values than the crude mortality rate because gastric carcinomas given as the secondary lesion as well as the primary diagnosis were accepted as autopsy cases in this analysis. Autopsy cases whose gastric carcinoma had been surgically removed and for which the diagnosis could not be histologically confirmed were excluded. This might result in an underestimation of true frequency. It is difficult to explain the difference in the proportion of gastric carcinoma in relation to radiation dose noted between Hiroshima and Nagasaki other than to say that it may be related to different demographic or other intrinsic factors. Generally, it is well known that age is involved in the development of tumors. The relative risk (200+ rad/0 rad) was high for gastric carcinoma in those who were aged 50+ years ATB in the period 1961-64, and the risk declined subsequently. However, for those under age 40 ATB, the relative risk was highest in the period 1969-74. Although nothing definite can be said solely on this basis, it may be that the carcinogenic effect of radiation is not clearly manifested until the cancer age is attained. The finding in the present study of a statistically significant greater degree of extension of gastric carcinoma cells in the gastric wall and a slightly increased degree of metastasis to the lymph nodes in the high dose group implicates irradiation at the higher dose levels.

訂正胃癌死亡率の算定数式は、

$$\text{訂正胃癌死亡率: } \frac{D_1 \times \frac{a}{A_1} + D_2 \times \frac{b}{A_2}}{N}$$

N: 対象総数

a, b, A₁, A₂, D₁, D₂: (研究対象および方法を参照)

訂正胃癌死亡率が粗胃癌死亡率より高い値を示しているのは、剖検例において主要診断のみならず、副病変としての胃癌をも採り上げたことによる。胃癌が外科的に摘出され、組織学的に診断を確かめることができなかった症例は除外した。このため実際の症例数よりも少ない可能性がある。胃癌有病割合と放射線量との関係でみられる広島・長崎の差は地域差、あるいは固有の差というより以外に意味付けは困難である。一般に腫瘍の発生には年齢が関係することはよく知られている。被爆時50歳以上であった胃癌剖検例は、1961-64年の期間に相対危険度(200 rad以上群/0 rad群)が高く、それ以降は低くなっている。これとは逆に、被爆時40歳未満であった群は1969-74年の期間が相対危険度は高い。このことのみで明確なことを述べることはできないが、放射線の胃癌に対する影響は癌年齢に達して初めて現われるものかも知れない。本研究において、高線量群ほど胃癌細胞の胃壁内での深達度が統計学的に有意に高く、リンパ節への転移度がわずかに高いのは、高線量に被曝したことによるものと思われる。

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