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乳腺症と乳癌

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特集 知っておきたい乳房管理の実際

乳腺症と乳癌

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乳腺症は臨床的にも，病理学的にも多様な病態を含む疾患である．その本質は乳腺に増殖，化生，退行などの変化が生じた状態で，ほとんどは正常からの逸脱と考えられるが，一部には異型乳管過形成（ADH）等の増殖性の病変をともなった，乳癌の危険率の上昇が報告されている病態も含まれる．ADHは非浸潤性乳管癌（DCIS）との関連が取りざたされており，その取り扱いには専門的な知識を要する．臨床上腫瘤や硬結を認めるものは，癌との診断に苦慮するものも少なくなく，乳腺専門医の元での適切なフォローアップが必要である．

Key Words 乳腺症，乳癌，異型乳管過形成（ADH），増殖性病変

はじめに

日常診療のなかで，一番多く遭遇する乳腺疾患といえば，まず乳腺症があげられるであろう．その臨床的病態は多岐にわたり，腫瘤の触知，乳房の硬結，乳頭分泌，乳房痛等を主訴として外来を訪れることが多く，ときとして癌との鑑別診断に苦慮する症例も少なくない．

癌との鑑別については，画像診断が中心となるが，詳細は他稿に譲るとして，本稿では乳腺症と癌の関連について病理学的考察を中心に述べて行きたい．

原因と疾患概念

冒頭で「乳腺疾患」という言葉を使ったが，はたして乳腺症は真の意味での「疾患」なのであろうか？．

乳腺症の原因は一般にエストロゲンの相対的過剰状態であると説明される．乳腺に対して，エストロゲンとプロゲステロンは協調的に影響を与えあっているが，ホルモンの不均衡によって乳腺に増殖，化生，退行などの変化が複雑に絡み合った状態が生じ，その多彩な組織像のそれぞれが乳腺症の本体であると考えられている．しかしながら，もともと乳腺は，その発達，成熟，退縮のすべての局面で，エストロゲンとプロゲステロンの影響下にあり，ホルモンバランスの不均衡によって引き起こされる乳腺症の状態も，広い意味では女性の生理的な加齢現象の，途中経過的な一つの側面であると考えられる．このような意味から，1990年代にANDI（aberrations of normal development and involution）「発達および退縮の正常からの逸脱」という概念が提唱され，乳腺症の疾患としての考え方に変化をもたらした[1]．

以前，Fibrocystic Diseaseと呼ばれていた病態が，最近ではFibrocystic ChangeまたはFibrocystic Conditionと表記されるように変化してきたのも，この流れに沿ったものである．つまり，乳腺

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症は一部のものを除いては疾患ではなく，正常もしくは一時的な逸脱であり，さらに変化の強いもののみが疾患として治療されるべきであるという概念は，乳腺症を診断，治療する医師は十分理解しておくべきであろう．

乳腺症の臨床像

池田らの報告によれば[2]，乳腺症の他覚的所見は，腫瘤触知38%，硬結触知47.5%であった．また，自覚症状として疼痛のみを認めるものは約10%に見られ，これらに加え圧痛をともなう腫瘤，硬結が約30%であった．乳頭分泌も３%に見られた．

乳癌検診を受診した女性が乳腺症と診断される割合は，報告者によりまちまちで，要精検例の9.7〜72.9%である．このような大きな差があるのは，乳腺症の定義や診断基準が不明瞭で，乳房硬結，疼痛，分泌などの症状に安易に乳腺症の診断名が用いられていることが原因と考えられる．

一般の診療や検診の現場において問題となるのは，乳腺症と乳癌との鑑別診断である．癌を乳腺症と誤診して適切な治療の時期を逸する事態は，何としてでも避けなければならない．現実には癌との鑑別困難な乳腺症があることも事実であり，どのような所見があれば専門機関に紹介すべきかのガイドラインが必要である．

Cochrane，Mansel ら[3]の提唱する基準を参考までに表１に掲げておく．大事な点は，乳腺専門医でない検診医が患者を診察する場合，所見の有る無しで患者を選別する「検診」は行っても，所見のある患者の「診断」は専門医に委ねることが重要であり，悲劇的な医療過誤を防ぐためにも検診から診断への円滑な連携のシステム構築が望まれる．

乳腺症と癌発生危険率

先に述べた通り，乳腺症とは乳腺に増殖，化生，退行などの変化が複雑に絡み合った状態で，その病理学的な分類としては坂本分類[4]，Dupont らの分類[5]などが有名であり，研究者によって若干の相違がある．本稿では，Dupont，Page らの分類に基づいて，乳癌と乳腺症との関連を考察したい．

彼らは，乳腺症とその後の乳癌（浸潤癌）発生率との間には関連があり，乳腺症の病理学的構成成分の違いで，浸潤癌の発生率が異なっていることを報告している（表２）．乳腺症は，その増殖性の差から，非増殖性病変（nonproliferative lesion），異型をともなわない増殖性病変（proliferative lesions without atypia），異型をともなう増殖性病変（proliferative lesions with atypia）の３クラスに分類される．

表１　専門医に紹介すべき所見（Cochrane RA，1997[3]）

1．腫　瘤	
	a．新しいもしくは限局した腫瘤
	b．既存の硬結の中の新たな腫瘤
	c．月経後も残る非対称性の腫瘤
	d．膿瘍
	e．繰り返す嚢胞
2．疼　痛	
	a．腫瘤に合併する疼痛
	b．一般の薬やサポートブラ等でも制御できない疼痛
	c．閉経を過ぎても持続する片側性の疼痛
3．乳頭分泌	
	a．50歳以上の女性の分泌物
	b．50歳以下の血性分泌、単乳管からの持続性分泌
4．乳頭陥凹，乳頭湿疹	
5．皮膚の異常所見（えくぼ症状など）	
6．濃厚な家族歴	

表2　非乳癌患者の乳腺生検組織所見による浸潤性乳管癌発症の相対危険率
(Dupont WD, et al, 1985[5], 森谷卓也ほか, 2003[6])

非増殖生病変 (危険性なし)	アポクリン化生, 軽度の過形成 閉塞性腺症, 乳管拡張症
異型をともなわない増殖性病変 (軽度危険性：1.5～2倍)	硬化性腺症, 中～高度の過形成 乳頭腫, 触知可能な大きさの嚢胞
異型をともなう増殖性病変 (中等度危険性：4～5倍)	異型乳管過形成 (ADH) 異型小葉過形成 (ALH)

注) 乳腺生検の既往がない同年齢の女性と比較して, 10～20年後に浸潤癌が発症する相対危険率を示している. 終生の危険率ではない.

1. 非増殖性病変 (nonproliferative lesion)

浸潤性乳管癌の発生確率は一般の女性と変わらない病変とされ, アポクリン化生, 軽度の過形成, 閉塞性腺症, 乳管拡張症などがこれに含まれる.

2. 異型をともなわない増殖性病変 (proliferative lesions without atypia)

浸潤性乳管癌の発生確率は一般の女性よりやや高く, 1.5～2倍と推定される病変で, 硬化性腺症, 中～高度の過形成, 乳頭腫, 触知可能な大きさの嚢胞等がこの範疇に入る.

3. 異型をともなう増殖性病変 (proliferative lesions with atypia)

浸潤性乳管癌の発生確率はさらに高くなり, 一般女性の4～5倍と推定される病変で, 異型乳管過形成 (atypical ductal hyperplasia : ADH) 異型小葉過形成 (atypical lobular hyperplasia : ALH), などをさす.

ADHは, 非浸潤性乳管癌 (ductal carcinoma in situ : DCIS) と良性の乳管過形成との中間的な, 良悪性境界領域に相当する病変として扱われるが[6], 病理組織学的定義については, 乳管過形成や癌のように細胞配列や核所見等による特徴的な診断基準がある訳ではなく, 明らかな良性や悪性, とくにDCISからの除外診断によってなされている. すなわち「DCISの病理組織診断基準の一部を有するが, これを完全に満足していないもの」と定義される. またADHは, 非コメド型のDCISの周囲に存在する頻度が高く, この事実からもADHと乳癌との強い関連性がうかがえる.

ADHの生物学的特性については, さまざまな解析が行われており, X染色体を用いたクローナル解析では, ADHは癌と同様にモノクローナルな病変であった[7].

筆者らは, 同一標本内にADH, DCIS, 浸潤性乳管癌を含む切除例を用いて, それぞれの病変内のヘテロ接合性の消失 (loss of heterozygosity : LOH) の解析を行い, 同一乳腺内のADH, DCIS, 浸潤癌巣には共通のLOHがあり, さらにADH～DCIS～浸潤癌部となるにつれてLOHのlocusが増加していることを確認した[8].

この事実は, 乳癌の多段階発癌を考えるうえで, ADHはDCISの前癌病変であり, さらなる遺伝子異常の蓄積によって浸潤癌へと進行するモデルを指示するが, ADHと後日同一部位に発生した癌とのLOHは一致しなかったとの報告もあり[9], ADHを放置することによって, それ自体がDCISに進行するのか, ADHは単なる癌発生の危険因子であり, 癌には進展しないものなのか, 今後の検討課題である.

乳腺症のうち乳癌発生頻度の高い増殖性病変の頻度は, 森谷らの報告[10]によれば, 乳腺症と病理診断された生検標本243症例のうち, 軽度の危険群とされる異型をともなわない増殖性病変は, 109例 (45%) で, 異型をともなう増殖性病変は5例 (2%) であった.

一方Dupontら[5]は, 非増殖性病変が69.7%, 異型をともなわない増殖性病変が26.7%, 異型をともなう増殖性病変が3.6%であったと報告して

いる．両報告では，軽度の危険群の割合がかなり違った印象を与えてはいるが，森谷らの報告では乳管過形成を軽度～中等度～高度とは分けて分類していないため，危険性なしの群に含まれるべき軽度の乳管過形成が軽危険度群に含まれるために生じた違いと推測され，両報告はよく一致した結果を示している．つまり生検の適応となるような乳腺症でも，約7割は乳癌の発生危険率が一般の女性と同等であると考えられる．

しかしその一方で，生検を受けた3割の乳腺症には増殖性の病変が確認できた事実は，乳腺症を背景として持つ女性へ対する適切なフォローアップの重要性を示唆しているといえよう．

■3 生検の適応と follow up

乳腺症は乳癌のリスクが健常者に比べいくぶん高いことや，腫瘤や硬結を触知する例では，癌との鑑別が困難なことがあり，一般検診ではない外来診療として follow される必要がある．触診だけでは癌との鑑別はほとんど不可能なため，超音波診断，マンモグラフィーといった画像診断を定期的に施行する事が必要である．

筆者の施設では，超音波にて確認できる腫瘤性病変で，嚢胞などの明らかな良性疾患を除いては積極的に超音波ガイド下に穿刺吸引細胞診（Fine Needle Aspiration Biopsy Cytology：FNABC）を行っている．さらに，画像診断上癌を疑った症例で，FNABC で確定診断の得られなかった症例に対しては，超音波ガイド下の16G 針による針生検（Core Needle Biopsy：CNB）を行っている．CNB の導入によって外科的生検適応症例はかなり限られたものとなった．

超音波上，限局性の低エコー領域として認められる境界不明瞭，辺縁が不規則といった腫瘤像や拡張した乳管内の腫瘤，限局性の豹紋型を示すエコー像は，低悪性度の癌，ADH，乳管過形成などが考えられる[11]．これらの病変は，術中凍結切片による迅速診断では確定診断を得ることが困難であり，前もって外科的生検や CNB を行い，永久標本による確定診断を得た後に，治療方針を決定することが必要である．

マンモグラフィーが乳癌検診に導入されたことにより，非触知の早期乳癌症例が微細石灰化を所見として発見される例が増加している．筆者らの施設では，マンモグラフィー上のカテゴリー 3，または4に該当する石灰化で，超音波上位置の特定できないものに関しては，ステレオガイド下太針生検（マンモトーム）を施行し成果を上げている．

2001年5月から2003年1月までの間にマンモトーム生検を施行した49症例のうち，病理組織診に有効な標本の得られた症例は45症例であり，乳癌と判定されたものが14例（31%），ADH，ALH

表3　石灰化所見と癌の頻度

形態＼分布	微細円形	淡く不明瞭	多形性	線状分枝状	全体
びまん性領域性	－	－	－	－	－
集簇性	0 / 3 (0%)	2 /15 (13%)	5 /11 (45%)	－	7 /29 (24%)
区域性	1 / 4 (25%)	2 / 7 (29%)	3 / 4 (75%)	1 / 1 (100%)	7 /16 (44%)
全体	1 / 7 (14%)	4 /22 (18%)	8 /15 (53%)	1 / 1 (100%)	14/45 (31%)

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等の異型をともなう増殖性病変がそれぞれ1例ずつ（2.2%ずつ）であった．非悪性と判断された症例の多くは，腺症，小嚢胞，アポクリン化生，乳管過形成等の乳腺症の成分を含む組織像であった．石灰化の所見と癌の頻度を表3に示す．乳腺症に特徴的な石灰化は，両側びまん性または散在性に見られる微細円形の石灰化で，これは生検の対象とはならない．一般に微細円形の石灰化は乳腺症を含む良性病変に多い．また，淡く不明瞭な石灰化も集簇性に分布するものは腺症等の乳腺症である症例が多かった．

生検の適応となった症例で癌が除外されたもの，生検を施行するほどではないが癌も否定できない病変は，はじめは3ヵ月後に再来受診してもらい，その後の受診間隔を決定している．フォローアップは視触診，超音波診は受診時ごと，マンモグラフィーは6ヵ月～1年ごとに施行するのがフォローアップの中心であるが，必要に応じてABCやCNBを追加施行している．

結　語

乳腺症はその多様な臨床症状，多彩な病理組織像から，何らかの所見があり，かつ悪性ではない乳腺疾患に対して，あまりにも安易に病名として説明するうえでの道具として用いられている．その本質はANDIの概念で説明される「正常からの逸脱」であることは事実で，患者に対しいたずらに乳癌のリスクを強調した説明を行う必要はないと思われるが，少なくとも診療に携わる医師の側では乳腺症における疾患部分と，正常部分との境界をわきまえた，病態に応じた対処が重要である．

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THE INCREASE OF FEMALE BREAST CANCER INCIDENCE IN JAPAN: EMERGENCE OF BIRTH COHORT EFFECT

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During recent decades, breast cancer incidence has been increasing in Japan. According to the latest reports from several cancer registries in Japan, the breast has become the leading cancer site in female cancer incidence. To analyze the trend of breast cancer incidence in detail, we summarized female breast cancer incidence in Miyagi Prefecture, Japan during 1959–1997, and evaluated the period and cohort effect on breast cancer incidence using the age-period-cohort model. Age-specific and age-standardized rates have increased over successive calendar periods. Around 1980, an accelerated increase in these incidence rates took place. A full model including age, period and cohort was best fitted to the trend of incidence. In the model, the effects of period and cohort were statistically significant. The nonlinear effect for cohort indicates an increasing trend, beginning with the cohort in 1888–1897, and the nonlinear effect for period showed a clear increase in risk with calendar period. Furthermore, the full model including a linear component showed a steadily upward trend in the cohort effect. Based on our own epidemiologic studies previously conducted in Miyagi Prefecture, and other published reports, the cohort effect is likely to be related to the change in prevalence of women with risk factors such as low parity and insufficient breastfeeding. We believe that the emergence of the cohort effect is an important finding, although the period effect may also persist. The significant cohort effect may give a caution for continuous increase of breast cancer incidence in Japan.

Key words: *age-period-cohort model; breast cancer; cohort effect; incidence; period effect; risk factor; trend*

During the past several decades, trends in cancer incidence have changed in Japan. Among females, breast cancer incidence has been continuously increasing. According to the latest reports from several cancer registries in Japan, the breast has become the leading cancer site in female cancer incidence.[1] Figure 1 shows trends in main cancer sites among females reported by the Miyagi Prefectural Cancer Registry (MPCR).[2,3] On the other hand, life cycles and behaviors in Japanese women have also largely changed. Which lifestyle factor may contribute to the increased rate of female breast cancer attracts great attention. Thus, the trend in breast cancer incidence is an important public health concern in Japan.[4]

Previously, we analyzed the trend in female breast cancer incidence in Miyagi Prefecture, Japan during 1959–1987, and indicated the importance of a period effect.[5] At that time, although studies from the US and Nordic countries have reported significant cohort effects on breast cancer incidence,[6–8] a cohort effect on incidence has been uncertain in Japan. We concluded that it might still take some time before the cohort effect emerges.[5] In our present study, we updated the incidence rate to 1997 and reevaluated the period and cohort effects on breast cancer incidence. A regression model—an age-period-cohort model—was applied to disentangle period and cohort effects. We focused on whether a cohort effect is associated with the updated breast cancer incidence.

MATERIAL AND METHODS

Incidence data

Updated incidence data of female breast cancer were obtained from the MPCR. Miyagi Prefecture is located in the northern part of Japan. The MPCR, which was initiated in 1951 and reorganized in 1959, covers the entire prefecture. Cancer cases are registered from clinics and hospitals, radiology and pathology departments, autopsy records, mass screening records and death certificates. Cancer incidence data since 1959 have been stored and reported.[9]

The analysis was based on the incidence data for ages 30–79 between 1959 and 1997. In the early period, original incidence data from the MPCR were stratified by an unequally spaced time period. Thus, the incidence data have been divided into 9 time periods (1959–61, 1962–64, 1965–67, 1968–72, 1973–77, 1978–82, 1983–87, 1988–92 and 1993–97). Based on this original data, we calculated age-specific breast cancer incidence rates for 10 5-year age groups (30–34 to 75–79 years) by period. As a denominator, the population at mid-year of each period was used: in census years, census population, and in noncensus years, population estimated by linear interpolation using the censuses was adopted. To look into the overall trend, direct age standardization to the world population was also performed. During the 9 time periods, the percentage of breast cancer cases registered from death certificates was below 10%. The percentage of cases verified histopathologically has been increasing (1959, 66.7%; 1997, 91.4%).

Statistical methods

To investigate the effects of age, period and cohort on breast cancer incidence, age-period-cohort models were used.[10–12] The statistical method has also been described in our previous study.[5] In the analysis, it was assumed that the interval widths for age and period are equal; therefore, the above original incidence data for the 9 unequally spaced time periods was reorganized into 8 5-year time period groups including 1958, 1958–62, 1963–67, 1968–72, 1973–77, 1978–82, 1983–87, 1988–1992 and 1993–1997.[10] In this reorganization, we estimated the number of 1958–62 incidence cases by multiplying the number of 1959–1961 (3-year period) incidence cases and 5/3. The number of 1963–67 incidence

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cases was estimated by multiplying the number of combined 1962–64 and 1965–67 (6-year period) incidence cases and 5/6. Although not shown in the tables, the MPCR has also reported incidence rates during 1962–1967. From the reorganized incidence data, 17 synthetic overlapping birth cohorts (1878–87 to 1958–67) were constructed by combining age and time periods. Thus, model fitting was based on 10 5-year age groups, 8 5-year time periods and 17 overlapping birth cohorts of 10 years each.

A general form of the age-period-cohort model is

$$\log(\lambda_{ijk}) = \mu + \alpha_i + \pi_j + \gamma_k,$$

where λ_{ijk} is the rate in a particular category, i.e., $\lambda_{ijk} = d_{ijk}/n_{ijk}$ (d_{ijk}: number of breast cancer cases, n_{ijk}: person-years) and α_i represents age effects, π_j period effects and γ_k cohort effects.[10–12] To fit the model and estimate the parameters, we used the maximum likelihood method. The number of breast cancer cases in each category (numerator of the rate) was assumed to have a Poisson distribution, and person-years for each category (denominator) were fixed. The person-years were calculated by summing the population counts in the census year, and those in the noncensus years that were estimated by linear interpolation using the censuses. The modeling procedure was performed using the GLIM system.[13] In the GLIM program, the number of breast cancer cases, d_{ijk}, was specified as the y-variate, Poisson errors with log link and $\log(n_{ijk})$ as an offset and then the terms of age, period and cohort were fitted.[14,15] Among these terms, age was entered into all models.

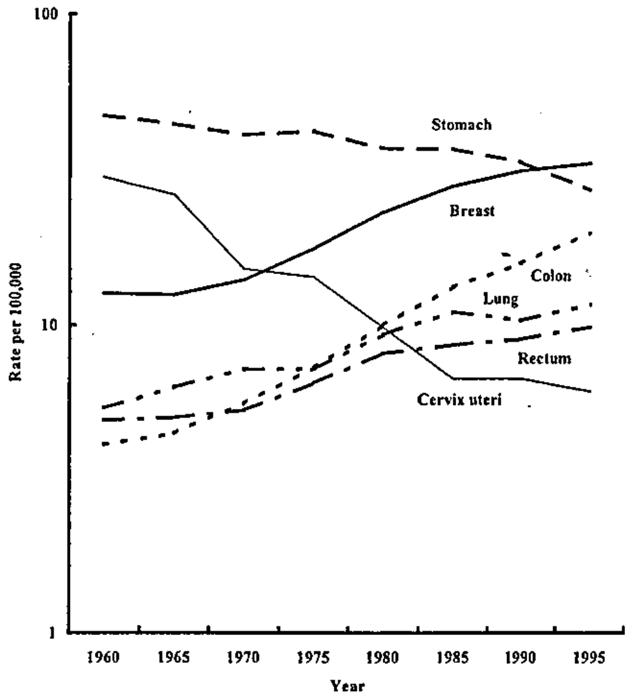

FIGURE 1 – Trends in age-standardized incidence rates for female leading cancers in Miyagi Prefecture, Japan, 1959–1997 (standard population: world population for all ages). The incidence rate of cervix uteri was calculated based on the corrected number of cases taking into account the number of part-unspecified uterine cancer cases.[5]

Usually, the variance in the statistical models is equal to the mean. However, because there are many potential sources of variation in population-based data like ours, the variance may be considerably larger than the mean (overdispersion). Therefore, the quasi-likelihood approach was applied, and the F-value as shown below was used for testing the statistical significance of each term.[6,16–18]

$$F = (\Delta G^2/\Delta df)/(G^2/df),$$

where G^2 and df are the Pearson chi-square and degree of freedom for the model, respectively, and ΔG^2 and Δdf the corresponding changes in the likelihood ratio statistic resulting from a parameter being dropped from the model.

The fit of different models compared to the age-model was judged based on adjusted R^2_A (adj-R^2_A).[6,7] This measure indicates how much of the variability is explained by factors other than age. For instance, the variability that period contributes is:

$$\text{adj-}R^2_A = 1 - \frac{G^2_{A+P}/df_{A+P}}{G^2_A/df_A}.$$

Regarding the problem in interpreting parameter estimates from age-period-cohort models, it is known that the age, period and cohort are linearly dependent. Ordinarily, it is not possible to disentangle the linear effects of the 3 terms (nonidentifiability problem). Only nonlinear effects for 3 terms can be uniquely defined.[10–12,15,19] Thus, we first estimated the nonlinear effects. The year of diagnosis 1958–62 and year of birth 1918–27 were taken as referent categories, and log (relative risk) by time period and birth cohort was calculated, respectively. Furthermore, in case the cohort effect was significant in the age-period-cohort model, we attempted to estimate the cohort effect including a linear component. Here we assumed that the linear period effect is zero.[10,12,19]

RESULTS

Age-specific and age-standardized incidence rates during 1959–1997

Trends in breast cancer incidence rates during 1959–97 are shown in Table I. The age-specific rate in each period shows a unique pattern; the rate stays constant following the reduction at around age 50–54, near the time of menopause.

TABLE I – BREAST CANCER INCIDENCE RATES BY AGE AND YEAR OF DIAGNOSIS PER 100,000 WOMEN IN MIYAGI PREFECTURE, JAPAN, 1959–1997

Age (years)	Year of diagnosis								
	1959–61	1962–64	1965–67	1968–72	1973–77	1978–82	1983–87	1988–92	1993–97
30–34	11.1	10.5	11.7	5.6	14.0	12.5	17.8	17.8	16.7
35–39	20.2	21.4	28.1	16.1	19.6	35.6	44.3	44.6	39.3
40–44	33.6	29.6	40.8	32.1	38.9	59.6	73.2	77.9	78.7
45–49	43.9	37.9	39.7	43.9	54.3	74.8	89.0	110.4	119.6
50–54	34.5	27.7	37.4	39.1	57.6	60.7	75.7	81.3	93.6
55–59	23.2	23.4	36.5	40.2	40.3	57.1	69.4	77.2	87.6
60–64	32.4	18.8	35.4	43.9	41.5	62.6	70.7	78.1	83.8
65–69	16.0	22.4	16.9	34.7	50.8	52.8	71.7	84.3	87.3
70–74	31.3	15.9	33.1	22.9	54.7	51.9	63.6	84.1	87.7
75–79	23.6	22.0	11.1	15.0	32.7	36.1	56.6	72.2	65.9
TASR[1]	27.5	23.8	30.8	29.8	38.8	50.6	62.4	70.4	74.0

[1]TASR, Truncated age-standardized incidence rate (direct age-standardization to the world population).

Age-specific and age-standardized rates have been continuously increasing since 1973, although the rate of increase was moderate during the earlier part of the period (1959–72). During the observation period, the age-standardized incidence rate increased 2.7 times.

Age-period-cohort model

The model fit to the breast cancer incidence is shown in Table II. First, we made a model containing a drift term.[11] However, this model gave a lower value for adj-R^2_A (0.88), and therefore was not adequate to describe the trend of incidence. Thus, we decided to consider an age-period, age-cohort and age-period-cohort model. Because the age-period-cohort modeling revealed some overdispersion in the submodel and full model, the effect of each term was evaluated based on the F-test, taking the value of adj-R^2_A into consideration.

While addition of the period to an age-cohort model gave a highly significant result ($p = 0.00013$), the addition of the cohort to an age-period model was also statistically significant ($p = 0.0299$). Furthermore, although the value of adj-R^2_A in the age-period model was larger than in the age-cohort model, the value of adj-R^2_A in the full model was larger than these submodels. We considered the fit of the full model to be better than the age-period and age-cohort models. Finally, the full model was used for summary description, which indicated that both the cohort and period effects might be associated with breast cancer incidence.

Figure 2 shows the nonlinear effects of period and cohort that were estimated by the full model. The relative risks by period effect steadily increased after 1968. The relative risks by birth cohort suggest an increasing trend, beginning with the cohort in 1888–1897.

Considering that the emergence of a cohort effect was an important phenomenon, we attempted to estimate the cohort effect including a linear component, assuming the zero slope of the period effect. Figure 3 shows the cohort effect estimated by this approach. The slope is smooth compared to Figure 2. The graph clearly indicates a steadily upward trend in the cohort effect since 1888.

DISCUSSION

The analysis of the 1959–1997 data from the Cancer Registry of Miyagi Prefecture, Japan revealed significant effects of period and cohort on female breast cancer incidence. In our previous analysis of the 1959–1987 data, although a significant period effect has been observed, the cohort effect has been unclear.[5] In this updated analysis, a cohort effect turned out to be significant. Around 1980, an accelerated increase in age-standardized incidence rates took place. Thus, addition of subsequent 10-year incidence data might make the cohort effect clear.

We compared the graph for the nonlinear period and cohort effects in the updated analysis with the previous one. Although the shape of the graph for the period effect has hardly changed, the graph for the nonlinear cohort effect in the updated analysis clearly showed an increasing trend by birth cohort. More recent generations may be exposed to a higher risk of breast cancer throughout their lifetime. To further investigate the cohort effect, we attempted to estimate the full cohort effect, including a linear component based on the assumption that the linear period effect has a zero slope. Although there is a possibility that the cohort effect including a linear component may be distorted by the true period slope, the graph for the full cohort effect is smooth and informative.[10,12] According to the full cohort effect, the upward trend in the cohort effect became clearer.

Epidemiologic studies of breast cancer have identified several risk factors. It is well known that reproductive factors are associated with the risk of breast cancer.[20–22] The unique pattern of age-specific rate shown in Table I, which has been called the Clemmesen's hook phenomenon, also suggests the importance of reproductive factors in the etiology of breast cancer. Our present findings on period and cohort effects may be due to changes in the prevalence of these risk factors. Also, the change in diagnostic procedures and the introduction of cancer screening may impact the trend in incidence.[23] Based on our own epidemiologic studies previously conducted in Miyagi Prefecture[22] and other published reports, we explored possible factors explaining the present period and cohort effects.

Table III presented risk factors selected from the review of previous studies[20,21,24] and our previous case-control study.[22] The case-control study is the only one that revealed risk factors for breast cancer in the population of Miyagi Prefecture. These risk factors indicate that women with late age at first birth or low parity are at a higher risk of breast cancer and that insufficient breastfeeding may be associated with the risk of breast cancer. Furthermore, it is suggested that women with early age at menarche may be at a higher risk, although the linear association with age at menarche was unclear in Miyagi Prefecture. First, we compared the cohort effect in our present study to the change in prevalence of these risk factors listed. The upper part of Table IV shows the trends in reproductive factors by birth year among women aged 40–64 as of 1990 in Miyagi Prefecture.[25] Although data presented in the table are limited to women with a birth year in 1926–1951, the trends in several reproductive factors are likely to parallel the birth cohort effect. Among them, parity number was a convincing risk factor in our case-control study, so the decrease of parity number in the recent generation may be related to the emergence of the cohort effect. The decrease in age at menarche is also likely to be related to the cohort effect. However, the most striking finding presented in Table IV is that the percentage of women choosing "breastfeeding only" has been rapidly declining. In other words, bottle feeding of milk has become widespread. Although the association with total lactation period was unclear in our case-control study, we considered that insufficient breastfeeding might be associated with the risk of breast cancer.[22] The decrease of both women choosing "breastfeeding only" and children breastfed (parity number) suggests that a large proportion of the cohort effect may be attributed to insufficient breastfeeding. Although most studies in developed countries have reported a weak association of breastfeeding with breast cancer risk at the individual level, insufficient breastfeeding might impact breast cancer incidence as a whole.[26,27] The comparison between the change in infant feeding method during the past several generations and the

TABLE II – SUMMARY STATISTICS FOR AGE-PERIOD-COHORT MODELS OF FEMALE BREAST CANCER, YEAR 1958–1997, [1]AGED 30–79 YEARS

Terms in model	Residual df	Residual G^2	Change[2] Δdf	Change[2] ΔG^2	F-test	adj-R^2_A
Age	70	1,534.80				
Age+drift	69	181.92				0.88
Age+period (AP)	63	120.07	15	47.00	2.06[3]	0.91
Age+cohort (AC)	54	126.35	6	53.27	5.83[4]	0.89
Age+period+cohort (APC)	48	73.07				0.93

[1]Original incidence data for the 9 unequally spaced time periods during 1959–1997 was reorganized into 8 five-year time period groups including 1958. The method for editing this data is described in Material and Methods.–[2]Comparisons between submodels and APC model.–[3]AP *vs.* APC, $p = 0.0299$, –[4]AC *vs.* APC, $p = 0.00013$.

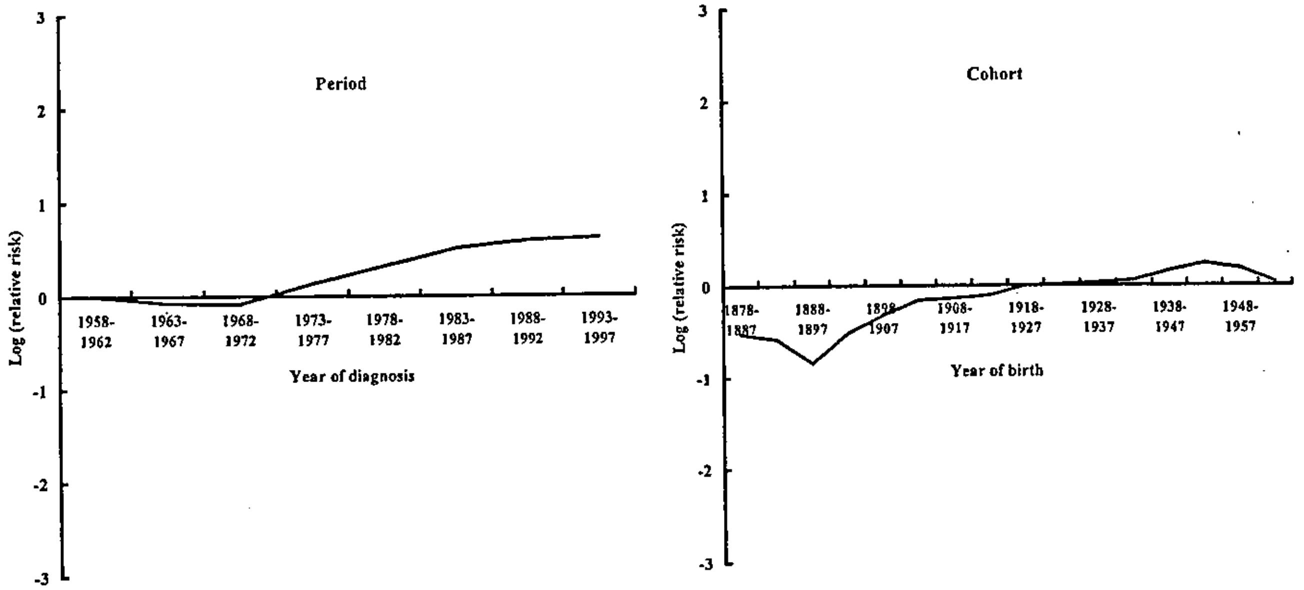

FIGURE 2 – Nonlinear effects of period and cohort on breast cancer incidence, based on age-period-cohort models.

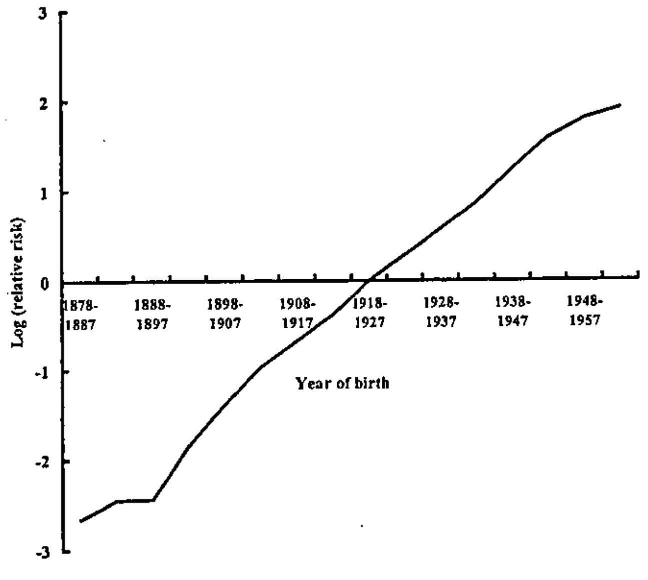

FIGURE 3 – Cohort effect on breast cancer incidence, based on full model including a linear component, assuming linear period effect being zero.

trend in breast cancer incidence may provide an important clue for clarifying the etiology of breast cancer.

Besides the reproductive factors mentioned above, some unknown factors may also be related to the cohort effect. We should consider the role of exogenous hormones such as oral contraceptives.[28] However, the Japanese government did not allow oral contraceptive use until 1998. Furthermore, the current or former usage rate of exogenous hormone among women aged 40–64 in Miyagi Prefecture was estimated to be 13.4% in 1990.[29] The effect of exogenous hormone on breast cancer incidence seems to be trivial in Japan.

In Table IV, body length and data including dietary intake from published reports[30,31] are also presented. The dietary data are from a cross-sectional national survey.[30] Body length has been increasing in recent generations, and intake of nutrients such as protein and fat has considerably changed during the past several decades. Previously, based on the suggestion given by Willett,[24,32] we hypothesized the relation of dietary intake with the trend in breast cancer incidence to be as follows: dietary habits might influence growth at an early age and endocrine events in life, and promote the cohort effect in the future.[5] In our present study, the cohort effect on breast cancer incidence became clear, corroborating this hypothesis. Although we could not obtain dietary data from the distant past, it is possible that the drastic change in nutrient intakes since the end of World War II, especially the increase in energy and protein intake, might have produced the increase in average body length. Some Japanese studies have also indicated the association of body length with the risk of postmenopausal breast cancer.[33] Although the associations between diet and breast cancer risk at the individual level are not fully investigated in Japanese population,[34,35] ecologic studies such as our study, i.e., long-term simultaneous observations of dietary habits and breast cancer incidence, may be a useful method for clarifying the role of dietary intake in breast cancer development.

Although we have emphasized the emergence of the cohort effect, factors related to the period effect also merit discussion. Statistical testing suggests that the period effect may be still stronger than the cohort effect. First, the relation between the period effect and increased diagnostic activities should be considered. In Japan, mammography was introduced in the 1960s and spread gradually. It is likely that the improvement in diagnostic instruments enhanced the period effect. Moreover, the introduction of screening programs may be related to the period effect. However, the participation rate in the screening has been low, as shown in Table IV,[31] and the impact of screening is likely to be small. Second, some other lifestyle factors may also be related to the period effect. In particular, the drastic change in nutrient intake may have contributed not only to the cohort effect but also to the period effect. Recent studies showed an association between high body mass index (BMI) and the increased risk of postmenopausal breast cancer.[33,35] Higher intake of calories or fat after World War II, as shown in Table IV, may have lead to the increase of obese women, which may have consequently increased postmenopausal breast cancer incidence. Although we could not obtain detailed data showing the relation of dietary intake and the BMI, it is likely that the change in dietary intake may partly explain the period effect.

TABLE III - RISK FACTORS FOR BREAST CANCER AND EVIDENCE FROM A CASE-CONTROL STUDY CONDUCTED IN MIYAGI PREFECTURE, JAPAN[1]

High risk	Evidence in Miyagi Prefecture[2]
Early age at menarche	Women with onset of menstruation at or after 16 years had a lower risk of breast cancer.
Late age at first birth	Women who gave birth to their first child at or after 30 years had a higher risk of breast cancer.
Low parity	With increasing parity number, the risk of breast cancer decreased.
Insufficient breastfeeding	Lactation for the last child reduced the risk of breast cancer. (The association with total lactation period is unknown.)
Tallness	–[3]
Obesity	–

[1]Risk factors were defined from the review of previous studies.[20,21,24] Factors which are considered to be related to the period and cohort effect were selected.–[2]Abstracted from reference [22].–[3]–, no data.

TABLE IV - TRENDS IN PREVALENCE OF RISK FACTORS AND OTHER RELATED FACTORS FOR BREAST CANCER

Factor	Year of birth					
	1926	1931	1936	1941	1946	1951
Data from the baseline survey of the Miyagi Cancer Study, 1990[1]						
Mean age at menarche (years)	15.7	15.9	15.0	14.6	14.0	13.6
Age at menarche ≥16 (%)	50.2	54.7	30.7	18.9	10.4	5.9
Mean age at first birth (years)	24.5	24.3	24.4	24.3	24.1	24.0
Age at first birth ≥30 (%)	7.8	6.4	4.9	4.9	5.2	7.6
Mean parity number	3.2	2.7	2.5	2.4	2.4	2.4
Nulliparous women (%)	2.0	1.4	2.9	2.7	3.0	3.4
Parity number ≥3 (%)	68.4	57.9	45.6	43.1	41.0	44.1
Women choosing "breastfeeding only" (%)	74.3	64.4	47.7	32.7	19.8	14.8
Mean body length (cm)	150.2	151.0	152.3	152.6	154.0	154.7

Factor	Calendar year									
	1950	1955	1960	1965	1970	1975	1980	1985	1990	1995
Data from published reports										
Nutrient intake per capita per day[2]										
Energy (Kcal)	2,098	2,104	2,096	2,184	2,210	2,226	2,119	2,088	2,026	2,042
Protein (g)	68.0	69.7	69.7	71.3	77.6	81.0	78.7	79.0	78.7	81.5
Fat (g)	18.0	20.3	24.7	36.0	46.5	55.2	55.6	56.9	56.9	59.9
Carbohydrate (g)	418.0	411.0	398.8	384.2	368.3	335.0	309.0	298.0	287.0	280.0
Participation rate in breast cancer screening program (%)[3]							3.4	4.8	7.1	7.6

[1]Data are from reference [25]. Baseline data obtained from 24,769 women aged 40–64 as of 1990 was analyzed.–[2]Data from the annual report of the cross-sectional national survey[30]. Nutrient intake for 1950 is estimated by the Standard Table of Food Composition in Japan, 1st edition, for 1955–1960 by the 2nd edition, for 1965–1970 by the 3rd edition and for 1975–1995 by the 4th edition, respectively.–[3]Data in Miyagi Prefecture.[31]

We consider that the significant cohort effect obtained in our present study is an important finding, although a strong period effect may persist. The emergence of a cohort effect may give caution for a continuous increase in breast cancer incidence. For instance, the total fertility rate is continuously declining in Japan: 1.76 in 1985 and 1.36 in 2000.[36] It is possible that such a change in reproductive behavior may lead to a further increase in breast cancer incidence.

In summary, our present analysis of breast cancer incidence updated to 1997 showed the emergence of a birth cohort effect. The period effect was also significant in the analysis. These period and cohort effects may be due to the changes in the prevalence of risk factors for breast cancer. Our present findings suggest that breast cancer incidence may continuously increase in future.

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The point of no return during the course of IgA nephropathy

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BACKGROUND

In 1993, D'Amico *et al.* reported seven patients followed a benign clinical course for 50 months or more but suddenly developed end-stage renal failure (ESRF) when the level of serum creatinine exceeded 2.5 mg/dL. Scholl *et al.* in 1999 described no remissions were observed in 22 progressive patients after exceeding 3.0 mg/dL creatinine. Hypertension and angiotensin-converting enzyme inhibitor (ACEi) treatment did not affect the course.

AIM/PATIENTS

We investigated the existence of a so-called 'point of no return' during the course of IgA nephropathy (IgAN); if serum creatinine exceeds the point, the renal function follows an irreversibly progressive course.

Nine hundreds and five patients of IgAN followed for longer than 8 years were divided into three groups regarding to the course of serum creatinine (Fig. 1).

RESULTS

In 732 patients (89%), serum creatinine did not exceed 1.3 mg/dL (stable forms). In 22 patients (2%), serum creatinine exceeded 1.3 mg/dL and was stabilized below 2.0 mg/dL during 5–15 years (burn-out forms) (Fig. 2). In 151 patients (17%), serum creatinine exceeded 2.0 mg/dL and then steadily increased in the rate of more than 0.05 mg/dL a year (progressive forms).

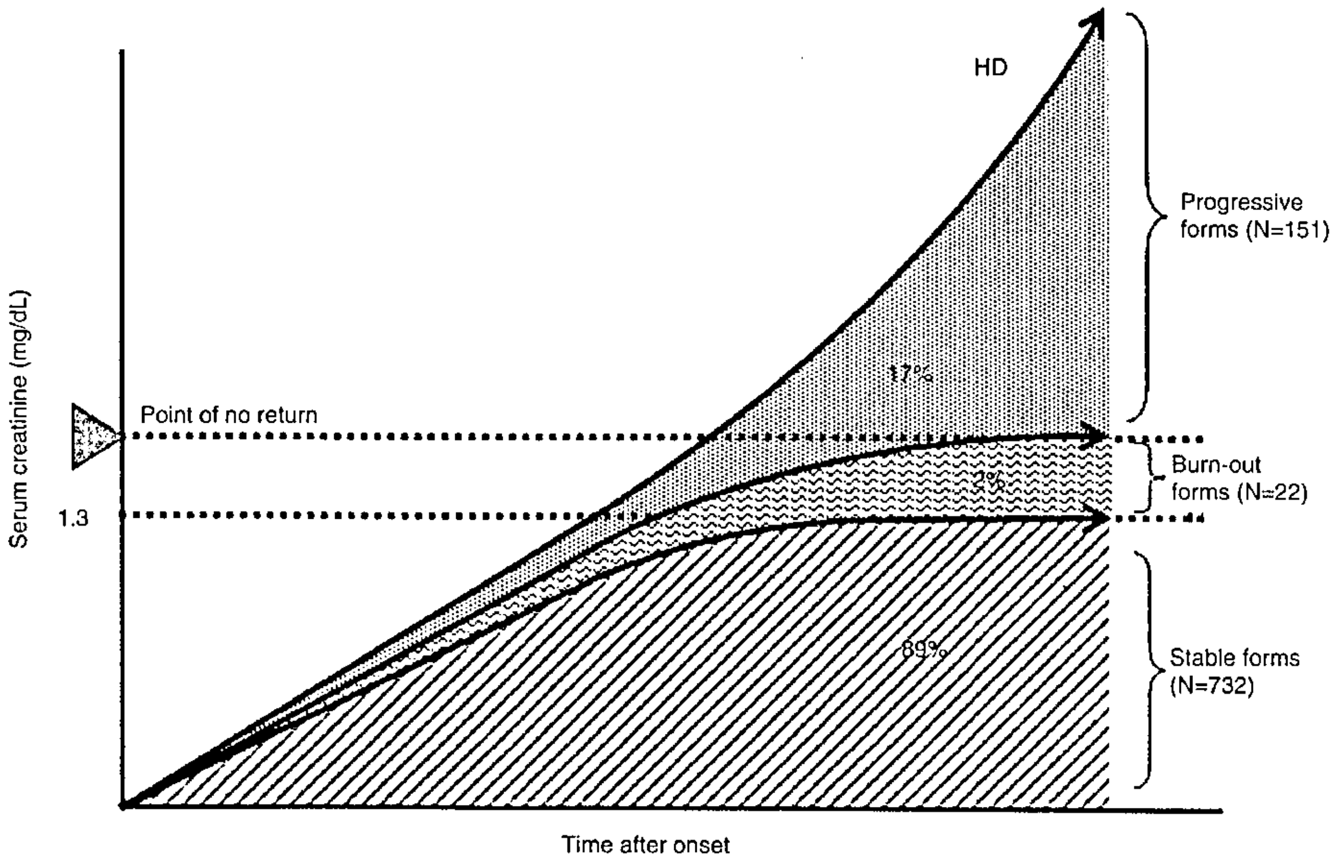

Fig. 1 Schematic graphs for the three forms of serum creatinine.

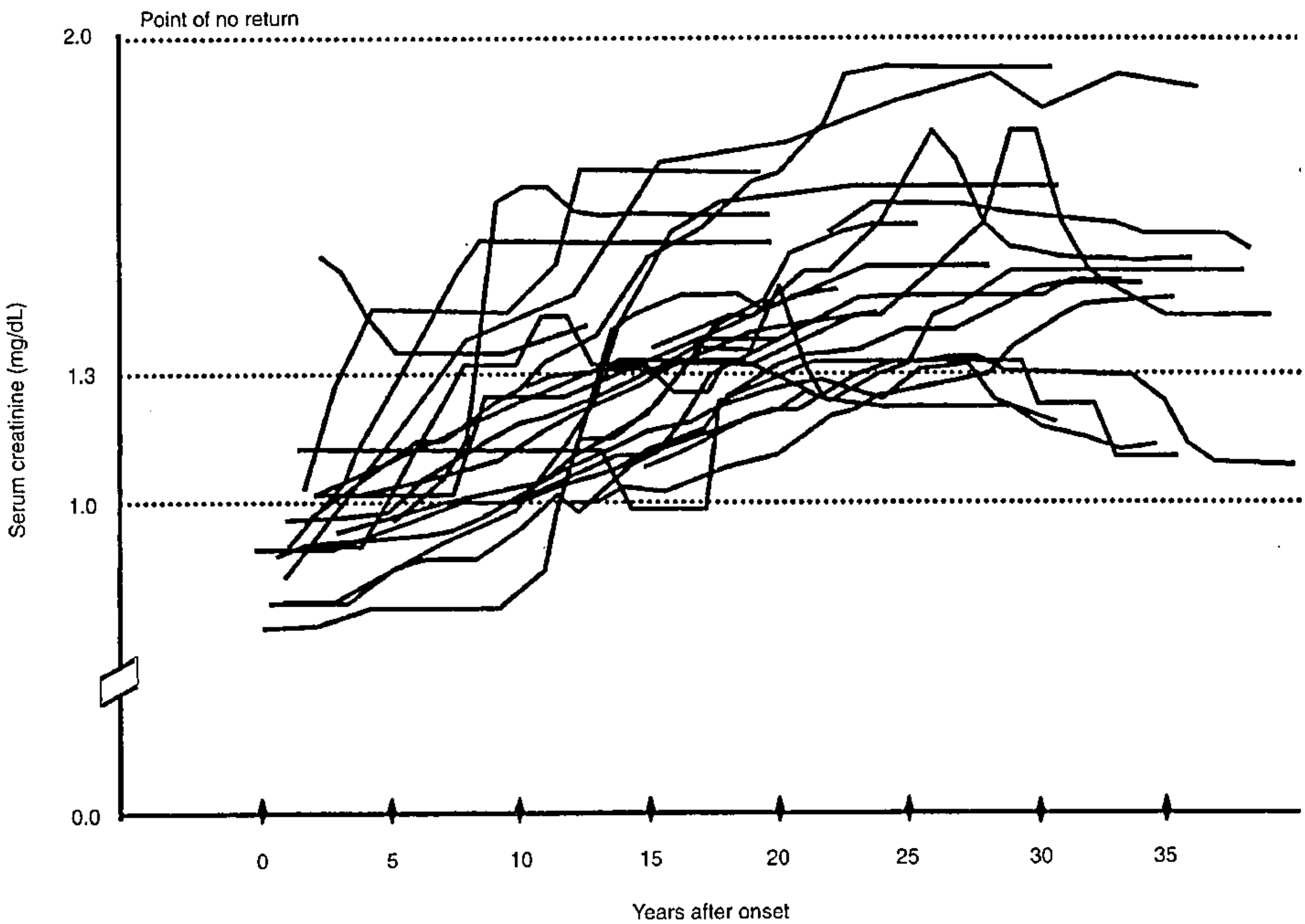

Fig. 2 Serum creatinine courses in burn-out forms (n = 22).

In patients with burn-out forms, 24 h-urinary protein excretion at the first visit and the last follow-up time was 1.1 ± 0.2 g and 0.6 ± 0.3 g, and serum creatinine was 1.1 ± 0.2 mg/dL and 1.5 ± 0.2 mg/dL, respectively. Negative urinary occult blood reaction was observed in 17 patients and mild microscopic haematuria (RBC < 0–4/vf) in other five patients. Active renal lesions such as cellular crescent and glomerular hypercellularity observed at the first biopsy were completely disappeared at the follow-up biopsy performed on the burn-out 18 patients.

Five patients of the burn-out form had been treated with corticosteroid, seven with antiplatelet drugs, and nine with ACEi.

In 151 patients with progressive forms, 12 patients considered to be a burn-out state with a negative urinary occult blood and scarred renal lesions proven by renal biopsies (burn-out type progressor). Mean daily urinary protein excretion was 0.6 g in the burn-out form and 1.7 g in the burn-out type progressor, and ACEi treatment was less frequent in the latter in which the time required for an increase from 2.0 mg/dL to 6.0 mg/dL serum creatinine ranged from 18 to 59 months. Four of 12 patients in burn-out type progressor treated with ACEi revealed slower decline in 1/Cr than the others (Fig. 3).

CONCLUSION

Our study confirmed that in IgAN a 'point of no return' existed at the serum level of 2.0 mg/dL. It was lower compared to the level of reported in two previous papers. The lowering may be due to the longer follow-up period in our study. Even if serum creatinine exceeded to this point, ACEi could double a timespan of increase in serum creatinine from 2.0 to 6.0 mg/dL in the patients of burn-out progressor.

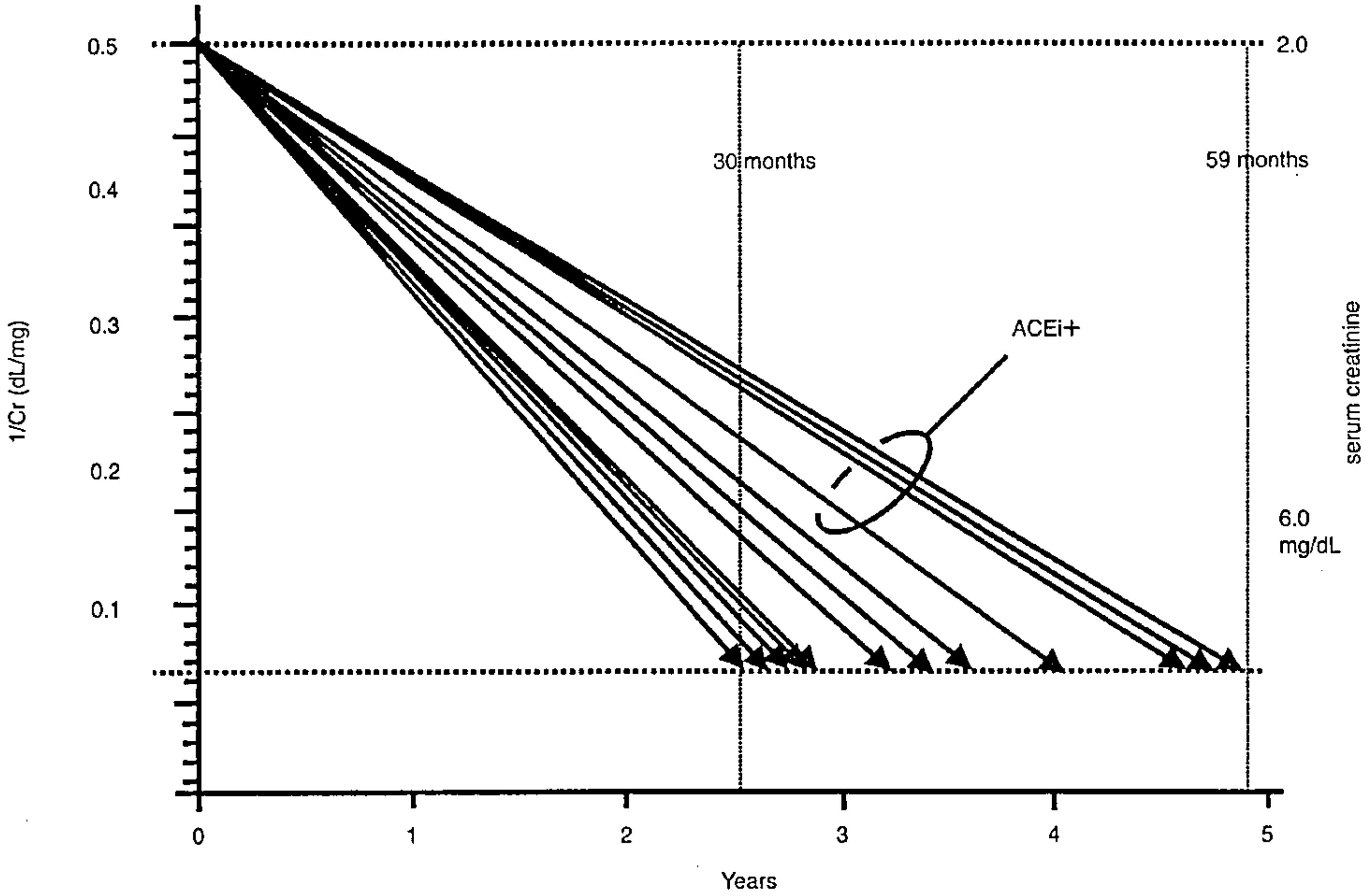

Fig. 3 Regression lie of the burn-out type progressor.

〈原　著〉

電子カルテ（Leafシステム）を短期間で導入できた要因と導入効果及び運用上の課題

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The factors of introducing an electronic medical record (Leaf system) in a short period of time, its introductory effects, and the point at issue.

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キーワード：電子カルテ、PDA、安全性

1 はじめに

厚生労働省は、2001年12月に保健医療分野の情報化にむけてのグランドデザイン[1]を策定し具体的な目標数値を設定して電子カルテの導入を推進しているが、なかなか普及が進んでいないのが現状である。原因として、導入に多額の費用がかかる、導入効果が明らかでない、準備に長期間を要する、院内のコンセンサスを得ることが難しい、などの問題が挙げられる。

盛岡赤十字病院（病床数：一般病床492床、一日平均患者数：入院430人・外来1,023人、職員数547名うち医師50名）では、国の電子カルテ補助事業を契機として部門システムの統合とオーダの拡充、診療情報の電子化などを目的に2002年1月に電子カルテの導入を決定。システム選定後7か月の準備期間で2003年1月から運用を開始した。紙カルテとの併用で電子化の範囲は狭いものの、1年間の運用したことにより、電子カルテの導入効果と運用上の課題が明らかになりつつある。

本論文では、当院における導入過程での取り組みと導入による効果、運用上の課題について報告する。

2 方　法

短期間で導入することができた要因について、当院での導入過程における取り組みを検証した。導入効果について、導入後に開催した院内導入報告会、院内報告、業務実績等を検証した。運用上の課題について、職員から提出された問題点に基づき委員会等で検討した事項から課題を検討した。

3 結　果

1）電子カルテシステム導入期間を短縮できた要因

（1）電子カルテ導入のコンセンサス形成

電子カルテの導入検討は、当院における最高意思決定機関である管理会議に、医事

システムが稼動後6年を経過し更新時期を迎えていること、医療の効率化や安全性向上に医療のIT化は必須であり予算の関係から導入範囲は狭いものの補助事業を活用して電子カルテの基盤を整備したい、との基本方針が示され導入の要否が諮られた。審議では多くの診療部長から積極的な意見が表明され、医師主導で電子カルテ導入を決定した。

その後のシステム選考においても、操作性に優れ画面展開が早く将来性もあるという医師の評価によりLeafシステムを選定した。

職員に対しては、導入決定時から随時情報を提供し、Leafシステムがグランドデザインの中で“情報化を有効活用した医療モデル”として提示されており、①携帯端末（以下PDA）による安全性の向上、②既存の部門システム統合による業務の効率化、③外来診療予約制による待ち時間対策、④医療行為が正確に記録されることによる医療の透明性の確保、⑤Webシステムで構築されており将来の地域医療連携が容易であることなど、病院や医療の抱える問題解決と将来性・拡張性に優れたシステム[2]であることを周知した。

(2) 導入方針の明確化

“優れたコンセプトの基に構築されたLeafシステムに運用を合わせ業務改革する”という基本方針を決定し、職員の理解が得られた。

(3) 導入検討機関の連携確保

検討機関は、各部門の運用を検討する6部会（電子カルテ、医事、処方注射、検査、食事、診療予約）、部会の調整を図る医療情報システム検討委員会（以下委員会）、予算措置等を含む最終決定を行なう電子カルテ導入推進本部（以下本部）の3階層とした。3階層間の連携を図るため、委員会の医師とシステム担当職員が本部と委員会に参加し6部会を分担することで3階層に2本のラインを確保した。更に委員会の委員が部会の幹事を分担し、電子カルテシステムベンダー（以下業者）も参加することで委員会と部会の間は4本のラインとした。委員会が6部会間の調整を担当したが、検討途中での整合性を確保するためシステム担当職員と業者が全ての部会に参加した。

部会の議事録と進捗管理表は業者が作成し、病院が確認することで認識の一致を図った。

(4) 参加意識高揚の為の広報活動、及び職員から指摘された問題点への速やかな対応

電子カルテ導入には医師の理解と積極的な活動が絶対条件であるとの院長判断から、常勤医師全員がいずれかの部会に参加した。

また、導入事業の成功には職員のベクトルを一致して取り組むことが重要であり、職員のモチベーションを高め、主体的に導入事業に参加できるよう意見収集と情報提供を行なった。2002年10月に電子カルテ運用方法案を全職員に文書で配布し、提出された質問にQ&A形式で回答し配布した。また、運用方法を具体的に人の動きとしてイメージし易くするため、自作のバーチャル運用ビデオを作成した。11・12月は3回のリハーサル毎に指摘された問題点や意見全てに対して改善方法や理由をQ&A形式で回答した。運用を開始した2003年1月は、本部と委員会の合同会議を連日開催して指摘された問題点の解決を図り速やかに伝達した。

2) 導入効果

(1) 診療情報の共有

診療記録は紙カルテと電子カルテの併用だが、病名・投薬・入院注射・検体検査・食事・入院基本情報が電子カルテで一元管理されることにより、これらの患者診療情報がリアルタイムで共有可能となった。

運用開始3ヶ月後に行った院内電子カルテ導入報告会での各部門報告によれば、診療上では医師相互の診療内容の把握が容易になり投薬・検査などの重複診療が減少した。

(2) 安全性の向上

前年の入院注射業務は、6月までは医師の手書き注射箋に基づいて病棟看護師が調剤し混注して実施、7月から12月は薬剤師が調剤し病棟看護師が混注して実施していた。現在は、オーダ入力（医師）→指示受け（看護師）→処方内容の監査・調剤（薬剤師）→調剤薬品の監査（薬剤師2名）→薬品と注射箋の照合（看護師2名）→混注（看護師）→注射の実施（看護師がPDAで確認）という流れになった。入院注射に関する安全性がこのようなシステムの変更とPDAの導入により、2002年に44件発生していた事例が導入後6ヶ月では1件のみと飛躍的に向上した（表1）。

表1　入院注射に関するアクシデント

	2002年 1月～6月	2002年 7月～12月	2003年 1月～6月
調剤者	病棟看護師	薬剤師	薬剤師
指示方法	注射箋	注射箋	オーダ入力
患者取り違え	4	7	1
実施漏れ	4	5	0
指示なし実施	3	0	0
混注漏れ	2	1	0
規格・単位違い	3	3	0
薬品違い	4	3	0
時間投与量違い	3	2	0
計	23	21	1

(3) 患者サービスの向上

当院で2001年9月に実施した外来患者アンケート調査（回収枚数1035）では、不満の第1位が『診察の待ち時間が長い』で52.7%、要望の第1位が『待ち時間を短くして欲しい』で70.0%、第2位が『予約制を実施してほしい』で29.4%

といずれも待ち時間に関する内容が主なものであった。

電子カルテ導入以前の予約診療は精神科のみで、その他は午前7時から受け付けていた。このため、診察順を確保しようと早朝4時台から患者が来院し始め、午前7時の受付開始時には平均78名（7.4%）が受付していたが、Leafシステムの診療予約機能に合わせて2003年2月から全科で予約制を導入したことによりこれらの早朝来院が解消された。また日中待合室で診察を待つ患者が3割程度まで減少し、診療待ち時間が改善した。

診察に遅れが生じると大型モニターに遅れ時間が表示されることから患者の待ち時間に関する問い合わせが減少し、看護師が検査等の患者説明を計画的にできるなど患者サービスの向上に繋がっている。

(4) 業務の効率化

既存の部門システム（臨床検査、薬袋印字、採取管準備、栄養管理）の統合（図1）とオーダ入力システムの拡充により伝票の搬送や再入力業務が減少した。また伝票の記載や伝達、転記や再入力に伴い発

生するミスとそれに伴うトラブルも減少した。これを時間外労働時間で評価すると、2003年4月から週休2日制となった違いはあるものの、前年比で一日平均患者数が入院2.0%・外来3.6%、職員数が0.8%増えている中で、全体で時間外が6.7%減少、増加している医師以外の職種では16.0%減少した（表2）。

薬剤部では処方・注射のオーダ入力充実により入院注射の薬剤師による調剤率が前年後半7割程度から88.5%に向上した。また全病棟へ薬剤師が行くことが可能となり、服薬指導件数も8月以降倍増した（図2）。

医事課では、4月からレセプト電算処理を開始し、医師による病名の登録とレセプトチェック機能により査定率（支払基金）が6ヶ月平均で昨年0.14%から今年0.08%と率にして41.5%減少した（図3）。

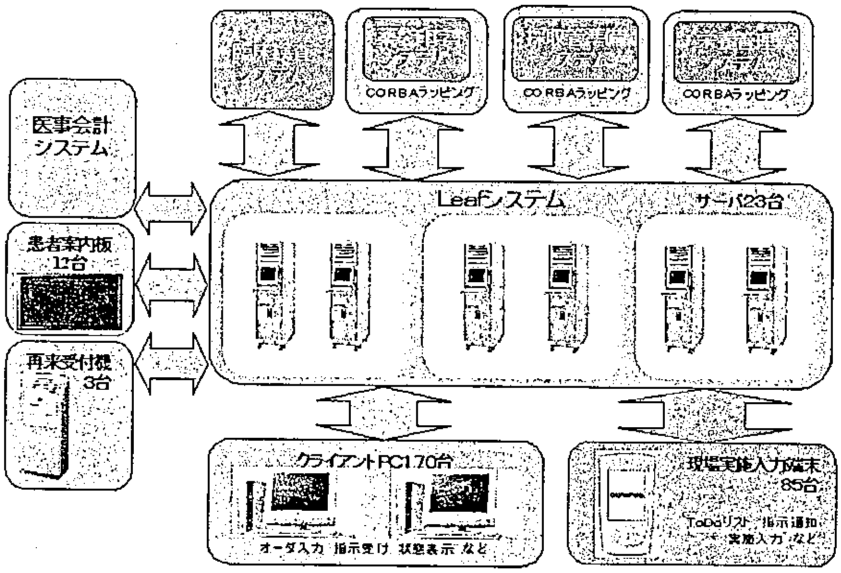
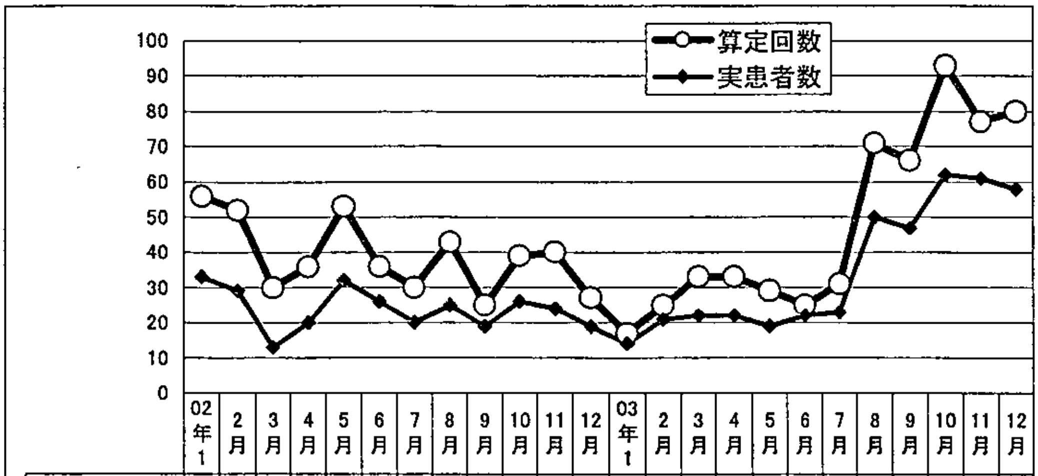


図1　システム構成図

表2　4・5・6月3ヶ月分時間外　前年比較

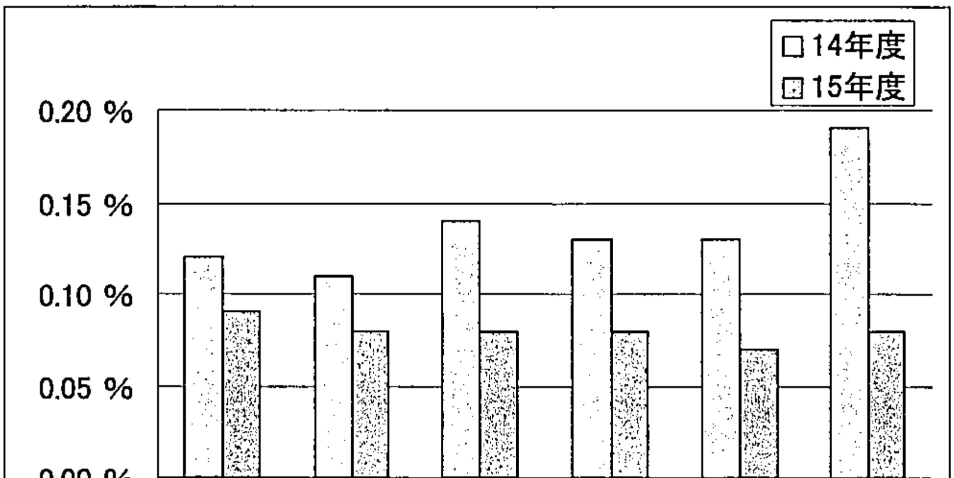
	2002年	2003年	増 減	%
入院患者数(平均)	421.3人	429.7人	8.4人	2.0 %
外来患者数(平均)	987.7人	1023.0人	35.3人	3.6 %
外来患者数(延べ)	66179人	63424人	−2755人	−4.2 %
職員数(平均)	524名	528名	4名	0.8 %
医 師	5446h 58m	6269h 56m	822h 58m	15.1 %
看護師	8841h 29m	7332h 16m	−1509h 13m	−17.1 %
医療職(二)	2250h 29m	2093h 20m	−157h 09m	−7.0 %
事 務	1450h 10m	1119h 35m	−330h 35m	−22.8 %
一般職(二)	153h 10m	114h 52m	−38h 18m	−25.0 %
計	18142h 16m	16929h 59m	−1212h 17m	−6.7 %
計(医師除き)	12695h 18m	10660h 03m	−2035h 15m	−16.0 %

※ 2002年は4週6休制、2003年は週休2日制
※ 看護学校と社会事業部及び2003年1月新設科を除く



	02年1	2月	3月	4月	5月	6月	7月	8月	9月	10月	11月	12月	03年1	2月	3月	4月	5月	6月	7月	8月	9月	10月	11月	12月
算定回数	56	52	30	36	53	36	30	43	25	39	40	27	17	25	33	33	29	25	31	71	66	93	77	80
実患者数	33	29	13	20	32	26	20	25	19	26	24	19	14	21	22	22	19	22	23	50	47	62	61	58

図2　月別服薬指導状況



	4月	5月	6月	7月	8月	9月
14年度	0.12	0.11	0.14	0.13	0.13	0.19
15年度	0.09	0.08	0.08	0.08	0.07	0.08

図3　査定率の前年比較（支払基金）

3）運用上の課題

（1）患者診療情報の一元化

診療情報が紙カルテと電子カルテに分かれているため、両方の情報を確認する必要がある。また、電子カルテが正本となる検査・薬歴等のデータについて、ベッドサイドでの確認が困難となっている。

（2）医師の業務負担の軽減

電子カルテはオーダ入力が指示となり、併せてカルテ記載となるため医師による入力が基本となる。このため医師の時間外が823時間（15.1％）増加しており、319時間は土曜日の回診分だが、残り504時間（9.3％）は入院患者の増加と厳格なオーダ入力の適用による負担増が原因となっている（表2）。