Evaluation of Anxiety and Salivary Chromogranin A Secretion in Women Receiving Breast Conserving Surgery Followed by Radiation Therapy

Kaori SEKI-NAKAMURA*, Katsuya MAEBAYASHI, Sachiko NASU-IZUMI, Tetsuo AKIMOTO and Norio MITSUHASHI

Breast cancer/Anxiety/Chromogranin A/State-Trait Anxiety Inventory (STAI)/Radiation.

We conducted a prospective study to assess the anxiety and salivary Chromogranin A (CgA), which is considered to be a biomarker of the stress response, in outpatients receiving breast conserving surgery followed by radiation therapy (RT) to the whole breast. Fifty consecutive patients who received whole-breast RT were enrolled in this study. The anxiety levels were measured by the State-Trait Anxiety Inventory (STAI) at the beginning of RT (baseline), 30 Gy, completion of RT, and 1 and 3 months after RT. Salivary CgA levels were also measured at the same time. The mean state anxiety score for all patients was 46.16 ± 1.57 at the beginning of RT (baseline) which continued to decline during and after RT. It reached its lowest score with 36.34 ± 1.56 at 3 months after RT (p < 0.0001). The mean trait anxiety score for all patients was 43.10 ± 1.54 at baseline and remained constant during RT but began to decline after completion of RT and reached a low level at 3 months after RT (p = 0.0021). The mean salivary CgA concentration for all patients demonstrated no consistent trends over time, but at 30 Gy the concentration showed a significant decreasing pattern (p = 0.0473). Salivary CgA concentrations and state anxiety and trait anxiety scores at all time points showed no correlation. The mean anxiety scores measured by STAI showed no positive correlation with salivary CgA concentration for breast cancer patients undergoing radiation therapy following breast conserving surgery.

INTRODUCTION

Anxiety is an unpleasant emotion affecting patients with cancer. Most patients before receiving radiation therapy (RT) have pre-treatment anxiety for uncertainty of RT, including radiation procedure, radiation exposure and potential adverse effects. Patients’ understanding of the illness and treatment can influence their ability to cope and adjust to RT. Exaggerated levels of anxiety before the beginning of RT may be maladaptive for the coping process which may even cause postponed RT or refusal of treatment. Therefore, correct assessment of patients’ anxiety is important. The State-Trait Anxiety Inventory (STAI) score is one of the subjective assessment tools for measuring anxiety levels. STAI consists of two separate, self-report scales for measuring the distinct concepts of state and trait anxiety. State anxiety can assess the temporary and situational anxiety accompanied with autonomic excitement, although trait anxiety measures the tendency of an individual’s response to stressful circumstances under conditions of increased anxiety.1,2) Ernstmann et al. reported that the state anxiety level measured by STAI is high compared to the reference data of non-cancer patients and the increase in anxiety was similar in both male and female patients.3) Chromogranin A (CgA) is a 48-kDa acidic glycoprotein stored and secreted by exocytosis from vesicles in the adrenal medulla and sympathetic nerves along with catecholamines. Salivary CgA is considered to be a biomarker of the stress response by the sympatho-adreno-medullary system with α-amylase.4,5) Nakane et al. demonstrated that salivary CgA-like immunoreactivity acutely increased in 9 adult male volunteers just before they made a public oral presentation compared with a control day.6) They also reported that CgA increased in 12 female students carrying out a word-processing task for 40 minutes. However other investigators have not found significant relationships between stress and salivary CgA level. There have been a few reports concerning the relationship between serum CgA level and stress for

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prostate cancer patients, but to our knowledge, no reports describing the correlation of serum or salivary CgA, and anxiety and stress for breast cancer have been found in the literatures.\textsuperscript{8,9}

A prospective study was therefore conducted for assessing the anxiety, salivary CgA and also correlation between them during RT and follow-up periods in outpatients receiving breast conserving surgery followed by whole breast radiation therapy.

MATERIALS AND METHODS

Patients
From August 2004 to April 2005, consecutive 50 patients who received breast conserving surgery followed by whole breast radiation therapy with a boost to the tumor bed without concurrent chemotherapy were enrolled in this study. Patients receiving hormone therapy were also allowed to participate. A written informed consent was obtained from all patients before participation. The study protocol was approved by the institutional review board at Tokyo Women’s Medical University.

Radiation Therapy
RT to the whole breast was administered using a tangential technique. Patients with risk factors including dominant intra-ductal spread, positive or closed surgical margin, or comedo type histopathologically were given a dose of 50 Gy/25 fr/5 weeks, and patients without risk factors were given a dose of 46 Gy/23 fr/4.6 weeks. Photon energy was 4 or 6 MeV. After tangential irradiation, 9 Gy/3 fr/ a week of radiation boost to the tumor bed with electron beams was administered. The electron beam was delivered by a rectangular or circular field with a size of 5–10 cm. In most cases, the electron energy was 6 or 9 MeV.

Self-report questionnaire (STAI questionnaire)
The Japanese version of the STAI questionnaire was used to assess changes in two different types of anxiety, namely, anxiety understood as the current state of an individual (“state anxiety”) and anxiety understood as a relatively stable trait of an individual’s personality (“trait anxiety”).\textsuperscript{10} Self-reported questionnaires were performed 5 times, prior to, during RT at 30 Gy, at completion of RT, and 1 and 3 months after RT.

Collection of saliva samples and measurement of salivary CgA
Saliva samples were collected by cotton-based techniques using a Salivette (Salstedt, Germany) or cotton swabs and centrifuged for 4 minutes at 2,500 rpm to remove the saliva from the cotton swab. The concentration of salivary CgA was measured in duplicates by enzyme-linked immunosorbent assay. Samples were quantified by colorimetric analysis at 450 nm. Saliva samples were collected at the same time the self-reported questionnaires were filled out.

Statistical analysis
Data are expressed as means ± standard error of the mean. The data for all measures were compared using an independent (Student) t-test for between-group differences. Changes between pre- vs. during or post-RT within groups were also measured using a paired t-test. Correlation between STAI score and salivary CgA concentration were assessed by Pearson correlation coefficient (GraphPad Prism, GraphPad Software Inc., San Diego, CA, USA). A value $p < 0.05$ was considered to indicate a significant difference.

RESULTS

Patient characteristics
Patient and tumor characteristics are shown in Table 1. The median age was 48.5 years ranging from 24 to 65 years. Forty eight patients had Performance Status (PS) 0 and 2 had PS 1. Forty seven patients (94%) received lumpectomy. Chemotherapy and hormone therapy was administered in 8 (16%) and 13 (26%) patients prior to RT, respectively. All patients were followed up periodically at least for 5 years.

Changes in state anxiety scores
Changes in mean state anxiety scores during and after RT are shown in Fig. 2. The mean state anxiety score for all patients was 46.16 with a standard error (SE) of 1.57 at the beginning of RT (baseline). The mean state anxiety score continued to decline during RT and reached a statistically significant level at 30 Gy of RT (p = 0.0074). The continuous decrease of in the mean state anxiety score could be observed after RT which reached its lowest score of 36.34 ± 1.56 at 3 months after RT (p < 0.0001).

Results of statistic analyses on patients’ and treatment characteristics of the mean state anxiety scores at each assessment point are shown in Table 2. Patients 50 years or older demonstrated a higher mean state anxiety score compared with patients under 49 years of age at 30 Gy irradiation (p = 0.0169).

The mean state anxiety scores in patients receiving quadrantectomy were higher at 3 months after RT compared with patients receiving lumpectomy (p = 0.0435). Patients who were going to receive adjuvant chemotherapy after RT demonstrated a significantly higher mean state anxiety score at 1 month after RT (p = 0.0118). No other patients’ and
Changes in mean trait anxiety scores during and after RT are shown in Fig. 2. The mean trait anxiety score for all patients was $43.10 \pm 1.54$ at the beginning of RT (baseline). The mean trait anxiety score remained constant during RT but began to decline after completion of RT and reached a statistically significant low level at 3 months after RT ($p = 0.0021$).

The results of the t-test analyses on the patients’ and treatment characteristics of the mean trait anxiety scores at each assessment point are shown in Table 3. Similar to the mean state anxiety score, patients over 50 years of age showed a higher mean trait anxiety score compared with patients under 49 years old at completion of radiation therapy and 3 months after RT ($p = 0.0152$, $p = 0.0045$).

Climacteric women demonstrated a higher mean trait anxiety score after RT with a statistically significant difference.
Table 2. The results of the t-test analyses on the patients’ and treatment characteristics of the mean state anxiety scores at each assessment point

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>pre RT (baseline)</th>
<th>30 Gy</th>
<th>post RT</th>
<th>1 month after RT</th>
<th>3 months after RT</th>
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<tr>
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</tr>
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</table>

NS: Not significant

Table 3. The results of the t-test analyses on the patients’ and treatment characteristics of the mean trait anxiety scores at each assessment point

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>pre RT (baseline)</th>
<th>30 Gy</th>
<th>post RT</th>
<th>1 month after RT</th>
<th>3 months after RT</th>
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</table>

NS: Not significant
at RT completion (p = 0.0496).

The mean trait anxiety score in patients receiving quadrantectomy were also higher at 3 months after RT. Patients receiving chemotherapy had a statistically significant higher mean trait anxiety score at 3 months after RT compared with those receiving no chemotherapy. Patients who were going to receive adjuvant chemotherapy after RT demonstrated a significantly higher mean trait anxiety score at the beginning of RT (baseline) (p = 0.0494). No other patients’ and treatment characteristics affected the mean trait anxiety score in the course of RT.

Changes in salivary CgA concentrations

Changes in mean salivary CgA concentrations during and after RT are shown in Fig. 3. The mean salivary CgA concentration for all patients was 3.2 ± 0.5 pmol/μl at the beginning of RT (baseline). There were no consistent trends in CgA concentrations over time, but at 30 Gy the concentrations showed a significant decreasing pattern (2.3 ± 0.4 pmol/μl) (p = 0.0473).

The results of the t-test analyses on the patients’ and treatment characteristics of the mean salivary CgA concentrations at each assessment point are shown in Table 4. At 3 months after RT, the mean salivary CgA concentration for the patients with stage II and III diseases was significantly higher compared with that of patients with stage 0 and I diseases (p = 0.0389).

![Fig. 3. Changes in means and standard errors of concentration of salivary Chromogranin A prior to, during and after radiation therapy.](image)

**Table 4.** The results of the t-test analyses on the patients’ and treatment characteristics of the salivary Chromogranin A concentrations at each assessment point

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>pre RT (baseline)</th>
<th>30 Gy</th>
<th>post RT</th>
<th>1 month after RT</th>
<th>3 months after RT</th>
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<td>Age</td>
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<tr>
<td>Clinical stage</td>
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<td>NS</td>
<td>p = 0.0389</td>
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<td>[Lumpectomy or Quadrantectomy]</td>
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<td>Hormone therapy</td>
<td>[Yes or No]</td>
<td>NS</td>
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Patients receiving axillary dissection had a significantly lower mean salivary CgA concentration only at the beginning of RT (baseline) compared with those receiving no axillary dissection ($p = 0.0041$).

Patients receiving neo-adjuvant chemotherapy had a statistically significant higher mean salivary CgA concentration at 30 Gy of RT compared with those receiving no neo-adjuvant chemotherapy ($p = 0.0215$). No other patients’ and treatment characteristics affected the mean salivary CgA concentrations in the course of RT.

**Correlations between state anxiety, trait anxiety and salivary CgA**

The state anxiety and trait anxiety measures at all time points were significantly correlated (at the beginning of RT: $r = 0.552$, $p < 0.0001$, at 30 Gy: $r = 0.754$, $p < 0.0001$, at completion of RT: $r = 0.762$, $p < 0.0001$, at 1 month after RT: $r = 0.773$, $p < 0.0001$, at 3 months after RT: $r = 0.776$, $p < 0.0001$) (Figs. 4 and 5).

Salivary CgA concentrations and state anxiety and trait anxiety scores at all time points, however, were not correlated (State anxiety; at beginning of RT: $r = -0.024$, $p = 0.870$, at 30 Gy: $r = 0.105$, $p = 0.484$, at completion of RT: $r = 0.010$, $p = 0.946$, at 1 Mo, after RT: $r = 0.045$, $p = 0.779$, at 3 months after RT: $r = -0.257$, $p = 0.198$, Trait anxiety; at beginning of RT: $r = -0.103$, $p = 0.479$, at 30 Gy: $r = -0.001$, $p = 0.994$, at completion of RT: $r = -0.147$, $p = 0.331$, at 1 month after RT: $r = 0.029$, $p = 0.857$, at 3 months after RT: $r = -0.254$, $p = 0.194$). Figures 6 and 7 show a correlation between state anxiety and trait anxiety scores and salivary CgA concentrations at the beginning of RT.

Five patients showed extremely high salivary CgA concentrations which were above 8.5 pmol/μl, as shown in Figs. 6 and 7. The mean salivary CgA concentration for the 5 patients was 12.6 ± 3.5 pmol/μl. The salivary CgA concentration of all 5 patients continued to decrease during and

![Fig. 4. A correlation between trait-state anxiety score at the beginning of radiation therapy (baseline).](image)

![Fig. 5. A correlation between trait-state anxiety score at the completion of radiation therapy.](image)

![Fig. 6. A correlation between state anxiety score and salivary Chromogranin A concentration at the beginning of radiation therapy (baseline).](image)

![Fig. 7. A correlation between trait anxiety score and salivary Chromogranin A concentration at the beginning of radiation therapy (baseline).](image)
after RT. No trend in socio demographic or treatment characteristics were found except for age. The median age of the 5 patients was significantly older at 61 years old ranging from 49 to 63 years.

**DISCUSSION**

The STAI score is a subjective assessment method to evaluate the level of anxiety felt not only by healthy subjects but also cancer patients. Much research has been published on the evaluation of stress and anxiety for various cancer patients. However, the subjective evaluation methods become limited in value if patients fail to provide reliable answers. In contrast, alternative objective assessment methods such as salivary CgA, α-amylase or cortisol are not limited.

The state anxiety and trait anxiety scores at all time points were significantly correlated, suggesting that the perception of participants on the day of attendance (viz. state) was associated with their underlying trait anxiety. Janiszewska et al. reported that statistical analysis confirmed a significant relationship between trait anxiety and state anxiety.

There was no precise data about state anxiety and trait anxiety scores of Japanese middle-aged women. Hidano et al. reported that mean state anxiety and trait anxiety scores for Japanese female university and vocational school students were 43.96 ± 11.91 and 43.85 ± 9.47, respectively. Iwata et al. also reported that the mean state anxiety scores of Japanese workers were substantially higher than those of American workers primarily due to the much higher scores of Japanese workers in responding to the anxiety-absent items.

Trimmel et al. reported that the mean state anxiety scores for breast cancer patients was 45.48 prior to the first cycle of chemotherapy and 40.81 by the last cycle, having significantly declined in the course of chemotherapy. However, these scores are fairly high compared with Cassileth’s report (reduction from 39.5 to 35.5). In this study, the mean state anxiety and trait anxiety scores for early breast cancer patients were 46.16 ± 1.57 and 43.10 ± 1.54 at the beginning of RT (baseline) which were almost the same levels as Trimmel’s reports. We observed the continuous decrease in mean state anxiety scores during and after RT reaching its lowest score of 36.34 ± 1.56 at 3 months after RT. The decline in state anxiety scores was more markedly in our study compared with patients who received two cycles of chemotherapy reported by Cassileth et al. However, the mean trait anxiety score remained constant during RT although it began to decline after completion of RT and reached a statistically significant low level at 3 months after RT. Janiszewska et al. demonstrated that the highest state anxiety and trait anxiety scores were noticed in patients during the diagnostic phase and the lowest in a disease-free period for breast cancer patients. Andersen et al. reported that gynecologic cancer patients experiencing low anxiety before RT significantly increased in state anxiety during RT. In contrast, patients experiencing high anxiety before RT significantly experienced less state anxiety. There was no difference in state anxiety between the 2 groups after completion of RT. Den Qudsten et al. reported that high-scorers on trait anxiety or low-scorers on agreeableness tend to score lower on perceived social support.

In the present study, there was no relation between stage, marital status, working conditions and the number of children, and the state anxiety and trait anxiety levels. Patients 50 years or older demonstrated statistically significant higher mean state anxiety and trait anxiety scores compared with patients under 50 years of age. It has been demonstrated that socio demographic characteristics such as age, marital status, income level, educational status etc. may significantly affect the anxiety levels for western patients with breast cancer.

The extent of surgery slightly affected state anxiety and trait anxiety scores for primary lesions but not axillar lymph nodes. The mean state anxiety and trait anxiety scores in patients receiving quadrantectomy were high with a statistically significant difference at 3 months after RT compared with patients receiving lumpectomy. Fleissig et al. reported on the results of large prospective randomized controlled trial comparing sentinel node biopsy with standard axillary treatment in the management of patients with early breast cancer. They found that state anxiety and trait anxiety scores at baseline and during the trial did not vary by treatment group until 18 months after surgery.

Chemotherapy had an effect on the mean state and trait anxiety scores during the course of RT. Patients receiving adjuvant chemotherapy after RT had a statistically significant higher mean state anxiety scores at 1 month after RT, the period when they were just undergoing chemotherapy. Patients who were going to receive adjuvant chemotherapy after RT also demonstrated a significantly higher mean trait anxiety score at the beginning of RT. It can therefore be said that only adjuvant chemotherapy significantly affects mean trait anxiety scores at baseline.

Catecholamine and cortisol are well known as objective index of stress because the sympatho-adreno-medullary system responds to stress. CgA is stored in adrenal medulla and adrenergic neurons and co-released with catecholamine, but they are not always co-released. Nakane reported that catecholamine responds rather physical stress than psychological one. Moreover, catecholamine is measured from serum or urine, on the other hand, CgA is measured from saliva, which is less invasive and easier to sample. Although cortisol is able to measure from saliva, the response to stress is slow and slight compared with CgA. Salivary CgA is considered to be a candidate for new stress biomarkers which enables to evaluate psychological stress objectively, precisely and easily.
However, the usefulness of salivary CgA as a biomarker for assessing mental stress remains controversial. Nakane et al. reported that a word processing task significantly increased salivary CgA level. In contrast, Noto et al. reported that state anxiety was significantly correlated to salivary α-amylase but not to salivary CgA under mental arithmetic stress. Ng et al. was unsuccessful in demonstrating that mental stress induced by academic assessment increased salivary CgA.

The mean salivary CgA concentration decreased significantly at 30 Gy. A relationship between CgA concentration and stages was observed at 3 months after RT. Our attempt to demonstrate that socio demographic characteristics such as marital status, working conditions and menstrual status may significantly affect CgA levels was unsuccessful. Concerning the effects of treatment on salivary CgA levels, axillary dissection and neo-adjuvant chemotherapy had an effect on mean salivary CgA concentrations.

A circadian rhythm of salivary CgA has been investigated by some investigators. Hong et al. reported that salivary CgA level peaked at 7:00 a.m. (time of awakening), then decreased and were maintained at a low level throughout the day, increasing slightly at 5:30 p.m. Den et al. reported the same results of a circadian rhythm of salivary CgA. Hong et al. also said that those who under stressed situation lose their circadian rhythm especially at time of awakening. In this study, saliva samples were collected during 11:00 a.m. and 4:00 p.m. when salivary CgA level was kept low. This might be one of the reasons which made it difficult to detect the difference of the CgA level among the patients.

In this study, the state anxiety and trait anxiety scores did not correlate with salivary CgA concentration at all measured time points, suggesting that the anxiety experienced by the patients in this study may not have been strong enough to increase salivary CgA or show a correlation between STAI scores and salivary CgA. Further research is needed to clarify this correlation.

RT has the potential to cause significant anxiety and stress for cancer patients. However, effects of RT on stress have not yet been fully investigated. Stress and fear from lack of information about the procedure, potential adverse effects and outcome of RT can have a more serious impact for patients undergoing RT. Hagmark et al. reported that no relationship between levels of anxiety with information was found. But Thomas et al. noted that intensive information reduced stress for patients in particular, having lower levels of anxiety and depression. Recently, a prospective randomized phase III trial was performed to investigate the impact of intense information sessions for patients undergoing RT.

In conclusion, the mean state anxiety score showed a good correlation with the mean trait anxiety score but not salivary CgA concentration for early breast cancer patients undergoing radiation therapy following breast conserving surgery. Age affected anxiety levels but not salivary CgA concentration. Further research is needed to clarify the correlation between anxiety levels and salivary CgA concentrations and how they are affected by RT.

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REFERENCES

comes in thyroid cancer patients undergoing radioiodine remnant ablation (RRA) with recombinant human TSH (rhTSH): a randomized controlled study. Clin Endocrinol 71: 115–123.


