EFFECTS OF ADVERSE EVENTS ON QUALITY OF LIFE SCORES IN A RANDOMIZED CLINICAL TRIAL OF ADJUVANT CHEMOTHERAPY FOR BREAST CANCER PATIENTS: N-SAS BC 02

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Background

- With the rise in medical costs, cost-effective analyses (CEA) are considered a useful tool for decision-making on resource allocation
- CEA can have a particularly high usability in the anti-cancer drugs area
- For CEA, evaluation of quality of life (QOL) is one of the important items
- QOL and CEA are usually based on the sense of values of citizens
- However, little is known about the detailed relationship between patient-assessed QOL scores and physician-measured grades of adverse events.

N-SAS BC 02

- A national multicenter phase III randomized clinical trial: National Surgical Adjuvant Study of Breast Cancer-02
  - ➢ Patients enrolled between November 2001 and May 2003
  - ➢ Comparing 4 cycles of taxane (paclitaxel or docetaxel) chemotherapy followed by 4 cycles of anthracycline plus cyclophosphamide with 8 cycles of taxane
  - ➢ Series of QOL scores including EQ-5D and adverse events according to the National Cancer Institute - Common Toxicity Criteria（NCI-CTC Version 2.0）were collected

Objective

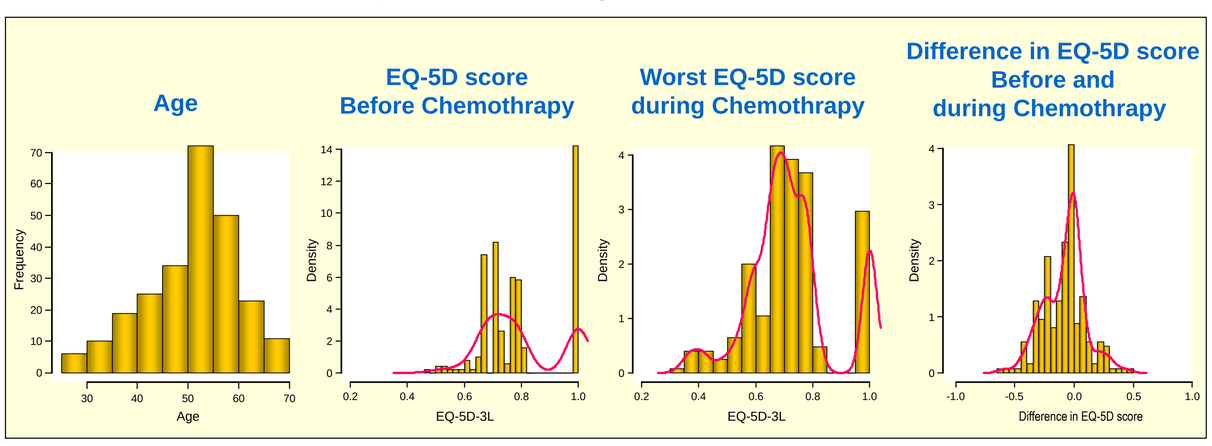
To investigate the effects of adverse events on quality of life (QOL) scores during adjuvant chemotherapy in breast cancer patients

Method

- N-SAS BC 02 database
- Linear regression model
- Objective variable: change in the EQ-5D score calculated as the worst scores (recorded three times during chemotherapy) minus baseline scores
  - ➢ Higher EQ-5D score indicate higher QOL
- Independent variables: incidences of adverse events recorded the worst scores by NCI-CTC set as binary variables regardless of their grades

Results

- Results of complete series of EQ-5D scores and complete adverse events data of 250 cases were adopted from the original data obtained from 300 cases
- Mean age : 51.4 (± 9.0) years
- Average EQ-5D score at baseline: 0.798 with bimodal peaks
- Average of the worst EQ-5D score in each participant during chemotherapy: 0.720
- Average change in EQ-5D score: -0.078 (range of -0.619 to +0.464)
  - 140 cases of QOL score deterioration
  - 54 cases of QOL score improvement



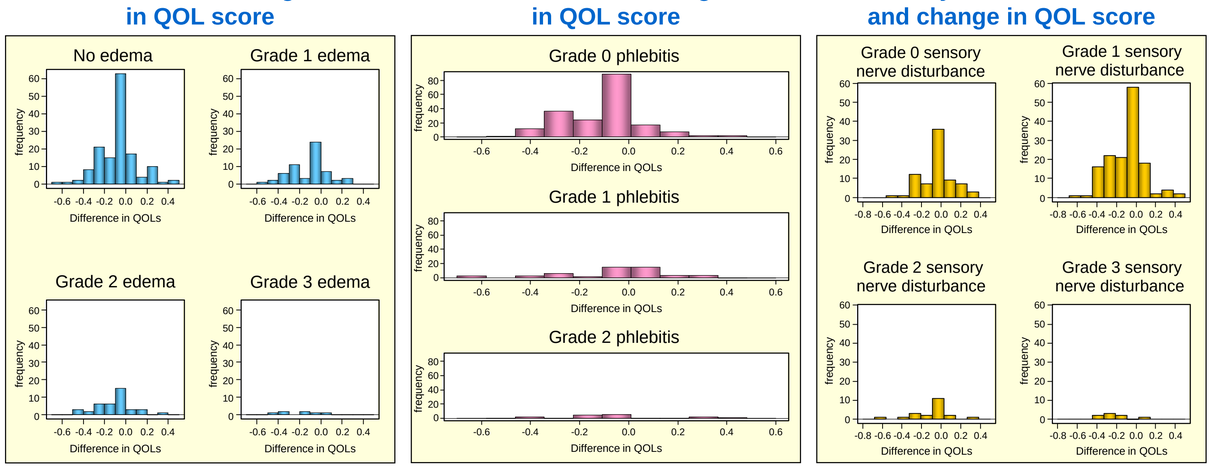
Adverse events

Case (Rate) Greyed item not used in regression model	None		Grade1		Grade2		Grade3		Grade4	
neutropenia	151	(60.4%)	45	(18.0%)	25	(10.0%)	20	(8.0%)	9	(3.6%)
leucopenia	165	(66.0%)	46	(18.4%)	33	(13.2%)	5	(2.0%)	1	(0.4%)
thrombopenia	245	(98.0%)	5	(2.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
anemia	133	(53.2%)	87	(34.8%)	29	(11.6%)	1	(0.4%)	0	(0.0%)
neutropenic fever	232	(92.8%)	-	-	-	-	18	(7.2%)	0	(0.0%)
edema	145	(58.0%)	59	(23.6%)	39	(15.6%)	7	(2.8%)	0	(0.0%)
non-malignant pleural effusion	246	(98.4%)	4	(1.6%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
non-malignant peritoneal effusion	250	(100.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
liver enzyme elevation	149	(59.6%)	83	(33.2%)	18	(7.2%)	0	(0.0%)	0	(0.0%)
bilirubin elevation	244	(97.6%)	6	(2.4%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
oral ulcer	142	(56.8%)	89	(35.6%)	18	(7.2%)	1	(0.4%)	0	(0.0%)
nausea	104	(41.6%)	106	(42.4%)	34	(13.6%)	6	(2.4%)	-	-
vomiting	176	(70.4%)	48	(19.2%)	19	(7.6%)	7	(2.8%)	0	(0.0%)
coprostasis	134	(53.6%)	81	(32.4%)	35	(14.0%)	0	(0.0%)	0	(0.0%)
diarrhea	187	(74.8%)	49	(19.6%)	11	(4.4%)	3	(1.2%)	0	(0.0%)
fatigue	72	(28.8%)	132	(52.8%)	42	(16.8%)	3	(1.2%)	1	(0.4%)
eye tearing	178	(71.2%)	69	(27.6%)	3	(1.2%)	0	(0.0%)	-	-
hair loss	7	(2.8%)	5	(2.0%)	238	(95.2%)	-	-	-	-
phlebitis	189	(75.6%)	47	(18.8%)	14	(5.6%)	0	(0.0%)	-	-
nail deformation	77	(30.8%)	156	(62.4%)	17	(6.8%)	-	-	-	-
sensory nerve disturbance	76	(30.4%)	145	(58.0%)	21	(8.4%)	8	(3.2%)	0	(0.0%)
frequent micturition	226	(90.4%)	22	(8.8%)	2	(0.8%)	0	(0.0%)	-	-
bloody urine	216	(86.4%)	33	(13.2%)	1	(0.4%)	0	(0.0%)	0	(0.0%)

Regression model

- Seventeen adverse events were selected as independent variables, excluding rare ones
- Three coefficients were significant (95% confidence interval)
  - Edema: -0.056(-0.106 ~ -0.006)
  - Phlebitis: 0.068(0.015 ~ 0.120)
  - Sensory nerve disturbance: -0.084(-0.133 ~ -0.034)
- R-square of this model : 0.118

Univariate analysis:



Discussion

- Three types of adverse events were related based on the regression model
- Phlebitis was associated with improved QOL scores
  - Univariate analysis showed that a small number of QOL improvement cases dragged the overall result
  - This is a relatively short-term adverse event, which consequently causes instability of the model
  - Statistically significant result, but it seems to be noise in the model
- Edema and sensory nerve disturbance cause relatively long-term effects, and thus possibly have an impact on QOL
- Limitations
  - The timing of assessing QOL and the timing of measuring adverse events were different in this trial
    - QOL was recorded at baseline and three times during chemotherapy
    - Adverse events were recorded as the worst scores by NCI-CTC during chemotherapy
  - The relevance of these factors could be weak
  - Examples of QOL improvement events may have reduced the model's descriptive power and caused a positive coefficient value
  - During chemotherapy, the QOL score could have improved due to recovery from the postoperative physical condition
  - In an adjuvant therapy environment, the average change in QOL scores may be small and sensitivity may be low

Conclusion

Since patients often suffer from sensory nerve disturbance and edema due to treatment with taxane-containing chemotherapy for a longer period, even after the termination of the chemotherapy, clinicians should selectively take care of these adverse events, avoiding deterioration of patients' QOL.

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