Title

Usefulness of Incisional Negative Pressure Wound Therapy for Decreasing Wound Complication Rates and Seroma Formation Following Breast Reconstruction Via Prepectoral Implant Insertion

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Short title

iNPWT in breast reconstruction

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Disclosure

No potential conflict of interest relevant to this article was reported.

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Short Title: PICO and Wound Complication Rates in Breast Reconstruction

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Abstract

Background: Seroma is a common complication in breast reconstruction via prepectoral implant insertion. PICO™ dressing, a type of incisional negative pressure wound therapy (iNPWT) is used to reduce complications postoperatively.

Methods: This study was a retrospective cohort study that included patients who underwent breast reconstruction via prepectoral implant insertion between February 2017 and July 2019. There were two groups, one that received PICO™ dressing and a control group. The frequencies of overall complications, major seromas, and re-operations were analyzed. The durations and total incidence of seromas were also analyzed.

Result: Sixty patients were included in this study (PICO™ : 37 and non- PICO™ patients: 23). The overall incidence of complications, major seromas, and frequency of re-operations was lower in the PICO group compared to the non- PICO™ group (18.9% vs. 52.2%, p=0.007; 16.2% vs. 43.5%, p=0.020; 2.7% vs. 26.1%, p=0.006, respectively). Univariate analysis was used to analyze the risk factors for complications due to the application of PICO™ dressing and showed statistically significant results for any complication. When univariate analysis was performed on risk factors for seroma, the duration of seroma showed statistical significance in association with PICO™ dressing status and mastectomy volume. The total number of patients who developed seroma were statistically correlated with age, PICO™ dressing status, and mastectomy volume.

Conclusions: PICO™ dressing after breast reconstruction could be a useful tool for reducing the frequency of complications and major seroma, as well as the duration and total incidences of seroma.

Level of Evidence: Level III

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Author contribution

Conceptualization: JD Yang, JY Ryu. Data curation: JY Ryu, JH Lee. Formal analysis: JY Ryu, JW Lee. Methodology: JS Lee, KY Choi. Project administration: HY Chung. Visualization: BC Cho. Writing - original draft: JY Ryu, JH Lee, JS Kim. Writing - review & editing: KY Choi, JD Yang. Approval of final manuscript: all authors.

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Introduction

In single-stage implant-based breast reconstruction, breast implants are inserted into the submuscular plane underneath the pectoralis major muscle. The implant needs to be inserted underneath the muscle because subdermal incision is not possible due to the need for soft tissue coverage [1]. Since the acellular dermal matrix (ADM) was first introduced in 2006, it is now possible to insert prepectoral implants during implant-based breast reconstruction [2]. ADM provides inferolateral support for the breast, thus there was decreased movement in the inferolateral direction during pectoralis muscle contractions, and soft tissue coverage was also possible when the implant was fully wrapped [2,3].

However, breast reconstruction via prepectoral implant insertion could lead to complications, such as seroma formation, surgical site infections, wound dehiscence, mastectomy skin flap necrosis, and implant extrusion, and adjuvant chemotherapy or radiotherapy may be needed, making patients uncomfortable [4].

Negative pressure wound therapy (NPWT) has been widely used on open wounds, and its utility has been proven in previous studies [5,6]. Recently, NPWT has also been used for closed surgical wounds and was shown to reduce wound complications, such as infections [6, 7]. The PICO™ dressing (Smith and Nephew, Hull, UK) is a portable incisional NPWT (iNPWT) device that can be used for closed surgical wounds.

The purpose of this study was to analyze wound complications, especially seroma formation, when PICO™ dressing was routinely used after breast reconstruction via prepectoral implant insertion, compared to those who did not receive PICO™ dressing.

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Methods

This study was a retrospective cohort, single-center study that included Korean patients who underwent immediate breast reconstruction via prepectoral implant insertion between February 2017 and July 2019. All patients underwent either skin-sparing or nipple-sparing mastectomy. Allogenic ADMs >2 mm thick were used in all patients. The study protocol was approved by the Institutional Review Board at our hospital on July 13, 2019 (No. 2019-06-016). Patient characteristics, including age, body mass index (BMI), smoking history, and medical comorbidities were collected from electronic medical records. Data on cancer status and the use of multimodal therapies included cancer stage, chemotherapy, and radiotherapy. Based on this, the patient cohort was divided into two groups: those who received PICO™ and those who did not.

The surgical technique used for breast reconstruction via prepectoral implant insertion was performed as previously described [3]. Postoperatively, classic treatment for incisional surgical wounds in some patients was performed using ointment and foam dressing. Wounds in other patients were treated using PICO™ dressings in the operation room postoperatively (See Video, Supplemental Digital Content 1). In the ward, if bleeding or oozing from the wounds were observed, dressings were changed to another type of PICO™ dressing. If there were no complications, dressings were changed three days and one week, postoperatively.

The frequency of each complication was assessed and recorded based on categories, including major seroma, surgical site infection (SSI), mastectomy skin flap necrosis, wound dehiscence, capsular contracture grade III or IV, hematoma, implant extrusion, and unplanned return to operation room (OR). If the patient experienced any of these complications, it was counted as 'Any Complication.' A major seroma was defined as the continuous outpouring of palpable fluid necessitating aspiration, as indicated by the clinician. In order to evaluate the duration of seromas, the postoperative day when final seroma aspiration was performed (A) and the duration of negative drainage after the surgery (B) were assessed. The duration of seromas was calculated as follows:

$$\text{Duration of seromas} = (A) - (B)$$

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The total volume of seroma aspirates were also evaluated.

Statistical analyses were conducted to compare the PICO™ group with the non- PICO™ group. Categorical variables were analyzed using Chi-squared test and Fisher's exact test. Continuous variables were analyzed by Student's *t*-test. Independent variables included PICO™ dressing status, overall complication rates, unplanned return to OR, and volume and duration of seroma. Thus, univariate multiple analyses were performed to investigate these independent variables. Logistic regression tests were conducted for categorical dependent variables and linear regression tests were used for continuous dependent variables. All these statistical analyses were performed using STATA, version 16.1 (StataCorp, College Station, Texas, USA). All data were considered statistically significant if their p-value was < 0.05.

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Results

We identified 60 patients who underwent breast reconstruction with prepectoral implant insertion. Immediately after the operation, 37 patients received PICO™ dressing, and 23 patients received classic ointment and foam dressing. The mean age of patients was 46.68 ± 7.73 (range, 26 to 67). The mean BMI of patients was 21.86 ± 2.42 kg/m^2 (range, 17.40 – 30.94 kg/m^2). All the patients were non-smokers and some patients had medical comorbidities, including hypertension (Table 1.). All patients had breast cancer. Forty-seven patients had stage I and 13 patients had stage II breast cancer. Among the patient cohort, 42 patients did not receive chemotherapy and the other 18 patients received adjuvant chemotherapy. Six patients received radiotherapy after the surgery (Table 2). Complications were assessed postoperatively: major seroma was investigated in 16 patients (26.67%), and unplanned return to OR occurred in 7 patients (11.6%), while other complications are described in Table 3.

The overall incidence of complications was lower in the PICO™ group compared to the non-PICO™ group, and this difference was statistically significant. The incidence of seroma, duration and volume of seroma (Table 5), and unplanned return to OR (Table 4) were also lower in the PICO™ group compared to the non- PICO™ group, and these were statistically significant.

Univariate analyses were used to analyze risk factors and revealed that other factors did not yield statistically significant results. However, the use of PICO™ dressing was statistically and significantly associated with any complication and mastectomy volume was associated with an unplanned return to OR. The use of PICO™ dressing incurred 0.128 times the risk of any complication compared to the non- PICO™ dressing, and when the mastectomy volume increased by 1 g, the risk of reoperation increased by 2.5%. (Table 6.).

When univariate analysis was performed on risk factors for seroma, the duration of seroma showed statistical significance in association with PICO™ dressing status and mastectomy volume. The

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duration of seroma decreased by 38.828 days when PICO™ dressing was used, and the duration increased by 0.111 days for each gram of increase in mastectomy volume. The indwelling time, which is the period when patients undergo negative drainage, was statistically significant only for BMI. As the BMI increased by 1 kg/m^2, the indwelling time increased by 0.425 days. The total volume of seroma aspirates was statistically significant when age, PICO™ dressing, and mastectomy volume were considered. An increase of age by 1 year translated to a 5.774 cc increase in seroma volume. In addition, the total volume of seroma decreased by 108.358cc in the PICO™ dressing group compared to the control group and the total volume of seroma increased by 0.473cc per gram increase in mastectomy volume (Table 7.). From the scatter plots for each patient, it was found that the duration of seroma was intensively distributed within 100 days when PICO™ dressing was used, and that the duration of seroma was distributed up to 200 days in case of the control group (Fig. 1).

Case

A 49-year-old woman underwent breast reconstruction via prepectoral implant insertion after nipple-sparing mastectomy on the left side. PICO™ dressing was utilized postoperatively and good cosmetic results without any notable complications were seen (Figure 2.).

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Discussion

PICO™ dressing, one of the iNPWT devices, was developed in 2011 to be used for closed surgical wounds. It induces a negative pressure (-80mmHg) using a small and light portable device and can be used for seven days. It is a convenient and semipermeable dressing, and the absorbed liquid is designed to evaporate [6,7]. The mechanism by which the PICO™ dressing acts on the wound is that it increases the surgical incision site blood flow, reduces the force applied to the surgical incision, and reduces the occurrence of hematoma or seroma by removing the lymph fluid surrounding the wound [8-11]. It was previously reported that PICO™ dressing reduces the incidence of complications in laparotomy, poststernotomy, and other surgical wounds localized in the lower leg [12-14]. However, there has been no report of the usefulness of PICO™ dressing for surgical wounds in breast reconstruction to date. We found that wound complication rates and seroma formations were reduced in patients who were treated with PICO™ dressing routinely after breast reconstruction via prepectoral implant insertion. First, the frequencies of the overall complications, major seromas, and reoperations were lower in the PICO™ dressing group as a result of analyzing categorical variables. All of these complications showed statistical significance. There were no statistically significant differences between the PICO™ group and the non- PICO™ group in terms of negative drainage but the PICO™ group showed a statistically significant decrease in terms of the duration and total volumes of seromas when categorical variables were assessed. In addition, univariate multiple variables analyses were performed to determine the risk factors, including the status of PICO™ dressing, for complication frequency and reoperation rate. Based on these results, the use of PICO™ was also statistically more significant than other factors. The odds ratio was 0.128 for the use of PICO™ dressing and this can be interpreted as a reduction of complications by 7.81 times (-1/0.128) when compared to non- PICO™ dressing. The reoperation rate was statistically more significant when based on mastectomy volume compared to PICO™ dressing status. In univariate multiple variable analysis, which was conducted to determine the risk factors for seroma, the use of PICO™ dressing and mastectomy volume had statistically significant effects on both

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duration and total volume of seroma. Age affected only the total volume of seroma.

The reason seromas occur in breast reconstruction via prepectoral implant insertion can be divided into the use of ADMs and the large pocket required for breast implants [15-17]. Three types of ADM were used in this study, CG CryoDerm (CGBio Co., Seongnam, Korea), MegaDerm (L&C Bio Co., Seongnam, Korea), and BellaCell HD™ (Hansbiomed Co., Seoul, Korea). Depending on the type of ADM, the duration and total volume of seroma may be affected but, as described in Table 4, there were no statistically significant differences between the groups divided by the type of ADMs and PICO™ dressing status. Therefore, in groups divided according to whether the PICO™ dressing was used or not, a specific ADM was not focused on a specific group; thus, bias was minimized in this study. The use of PICO™ dressing can reduce the large pocket required for breast implants, which may cause seroma. It may also minimize the dead space between pockets and implants through continuous negative pressure after surgery and allow for better drainage when negative pressure has already been applied. Upon removal of negative drainage, semipermeable dressing can be used to aid in the evaporation of the remaining seroma. However, in this study, the use of PICO™ dressing was not correlated with a reduction in the indwelling duration through negative drainage.

This study is a retrospective study, which is its main limitation. In addition, the sample size was small, which limits its generalizability. Biases could not be controlled, such as the use of ADMs as a single type, which can affect the duration and volume of seroma. The effect of the latter could not be elicited.

In conclusion, based on the results of this study, the use of PICO™ dressing after breast reconstruction via prepectoral implant insertion reduces the frequency of complications and the development of major seroma, as well as the duration and total volume of seroma. Other factors affecting the duration of seroma were mastectomy volume, and factors affecting the total volume of seroma included mastectomy volume and age, in addition to whether PICO™ dressing was applied or not.

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Ethical approval

The study was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital (IRB No. KNUCH 2019-06-016) and performed in accordance with the principles of the Declaration of Helsinki. Written informed consents were obtained.

Patient consent

The patients provided written informed consent for the publication and the use of their images.

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Figure Legends

Figure 1. Scatter plot for Duration of Seromas

The duration of seroma was intensively distributed within 100 days in case of PICO dressing. In non-PICO group, the duration of seroma was distributed up to 200 days.

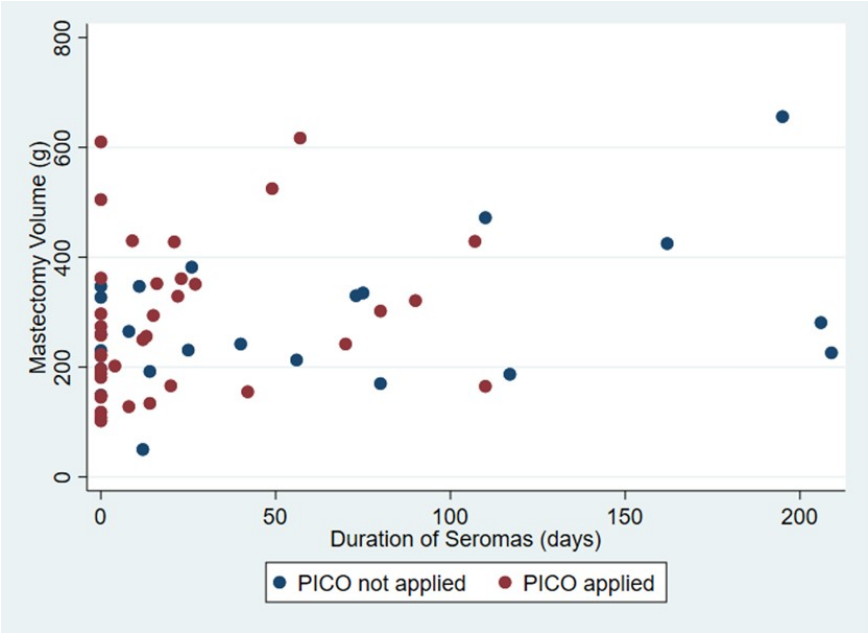

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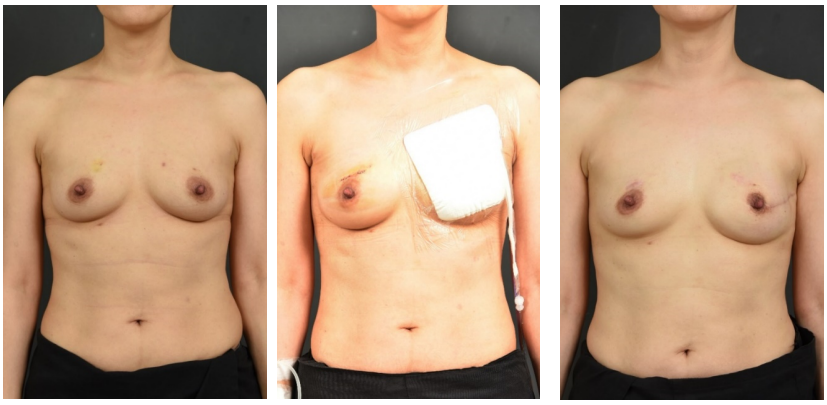
Figure 2. Case for appliance of PICO dressing

49-year-old woman with left-sided breast cancer. After nipple sparing mastectomy, breast reconstruction was performed via prepectoral implant insertion. Postoperative PICO™ dressing was conducted on the surgical incisional wound. (A) Preoperative view (B) 5 days of postoperative view (C) 1 year of postoperative view



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Tables

Table 1. Patient Demographics and Comorbidities

	Value (%)
No. of patients	60
Age at surgery	Mean 46.68 ± 7.73
<30 years	2 (3.3)
30-39 years	5 (8.3)
40-49 years	33 (55)
50-59 years	16 (26.6)
60-69 years	4 (6.6)
>70 years	0 (0)
BMI	Mean 21.86 ± 2.42
<18.5 kg/m^2	1 (1.6)
18.5-24.9 kg/m^2	54 (90)
25-29.9 kg/m^2	4 (6.6)
30-34.9 kg/m^2	1 (1.6)
>35 kg/m^2	0 (0)
Tobacco use	
No smoker	60 (100)
Former smoker	0 (0)
Current smoker	0 (0)

Medical comorbidities	
Hypertension	4 (6.6)
Diabetes	0 (0)
Coronary artery disease	0 (0)
DVT / PE	0 (0)
Connective tissue disease	0 (0)
Types of acellular dermal matrix	60 (100)
CG CryoDerm (CGBio Co., Seongnam, Korea)	35 (58.33)
MegaDerm (L&C Bio Co., Seongnam, Korea)	5 (8.33)
BellaCell HD^{TM} (Hansbiomed Co., Seoul, Korea)	20 (33.33)

Values are presented as number (%).

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Table 2. Cancer Characteristics and Multimodal Therapies

Characteristic	Value (%)
No. of patients	60
Cancer stage	
I	47 (78.3)
II	13 (21.6)
III	0 (0)
IV	0 (0)
Chemotherapy	
None	42 (70)
Neoadjuvant	0 (0)
Adjuvant	18 (30)
Radiotherapy	6 (10)

Values are presented as number (%).

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Table 3. Number of Complications

Complications	Value (%)
Major seroma	16 (26.67)
SSI	0 (0)
Mastectomy skin flap necrosis	1 (1.6)
Wound dehiscence	0 (0)
Capsular contracture grade III or IV	3 (5)
Hematoma	1 (1.6)
Implant extrusion	0 (0)
Unplanned return to OR	7 (11.6)

Values are presented as number (%).

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Table 4. Comparison of Complication Rates

	PICO group	Non-PICO group	P-value[a)]
Types of acellular dermal matrix			
CG CryoDerm	23 (62.16)	12 (52.17)	0.171
MegaDerm	1 (2.70)	4 (17.39)	
BioCell HD™	13 (35.16)	7 (30.43)	
Any complication [N (%)]			
Yes	7 (18.92)	12 (52.17)	0.007**
No	30 (81.08)	11 (47.83)	
Major seroma [N (%)]			
Yes	6 (16.22)	10 (43.48)	0.020*
No	31 (83.78)	13 (56.52)	
Unplanned return to OR [N (%)]			
Yes	1 (2.70)	6 (26.09)	0.010*
No	36 (97.30)	17 (73.91)	

Values are presented as number (%).

[a)] Chi-square test or Fisher's exact test.

* $p < 0.05$, ** $p < 0.01$

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Table 5. Comparison of Duration and Volumes of Seroma between PICO™ and non- PICO™ groups

	PICO group (N=37)	Non-PICO group (N=23)	P-value [a)]
Age (year)			
Mean	47	46.17	0.690
SD	1.37	1.42	
BMI (kg/m^2)			
Mean	21.56	22.33	0.235
SD	0.36	0.57	
Indwelling time (days)			
Mean	9.89	11.26	0.197
SD	0.49	0.92	
Duration of seromas (days)			
Mean	21.87	61.70	0.018*
SD	5.23	14.91	
Amounts of seromas (cc)			
Mean	53.89	189.65	0.019*
SD	15.27	51.94	

[a)] Student's t-test

* $p < 0.05$, ** $p < 0.01$

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Table 6. Univariate Analysis for Risk Factors for Complications

	Any Complication		Unplanned return to OR	
	Odds Ratio (95% CI)	P-value [a)]	Odds Ratio (95% CI)	P-value [b)]
Age	1.095 (0.988 – 1.215)	0.085	0.925 (0.748 – 1.143)	0.471
BMI	1.214 (0.881 – 1.672)	0.235	0.666 (0.355 – 1.250)	0.205
Hypertension	0.372 (0.018 – 7.606)	0.520	25.521 (0.322 – 2025.869)	0.147
Cancer stage II	1.010 (0.156 – 6.529)	0.992	4.418 (0.222 – 87.942)	0.330
Radiotherapy	4.551 (0.422 – 49.038)	0.212	4.283 (0.034 – 540.212)	0.556
Adjuvant Chemotherapy	2.449 (0.459 – 13.060)	0.294	3.284 (0.073 – 148.127)	0.541
PICO dressing	0.128 (0.025 – 0.660)	0.014*	0.001 (0.000 – 2.072)	0.075
Mastectomy volume	1.006 (1.000 – 1.013)	0.060	1.025 (1.002 – 1.048)	0.035*

[a), b)] Logistic regression with odds ratio for categorial variables

* $p < 0.05$, ** $p < 0.01$

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Table 7. Univariate Analysis for Risk Factors for Seromas

	Duration of Seromas		Indwelling Time		Total amount of Seromas	
	Coefficient (95% CI)	P-value [a)]	Coefficient (95% CI)	P-value [b)]	Coefficient (95% CI)	P-value [c)]
Age	1.506 (-0.308 – 3.320)	0.102	-0.018 (-0.149 – 0.114)	0.789	5.774 (0.154 – 11.395)	0.044*
BMI	5.485 (-0.343 – 11.312)	0.065	0.425 (0.003 – 0.846)	0.048*	13.688 (-4.369 – 31.745)	0.134
Hypertension	6.532 (-52.311 – 65.376)	0.825	4.241 (-0.014 – 8.497)	0.051	119.627 (-62.695 – 301.949)	0.194
Cancer stage II	-21.088 (-54.626 – 12.449)	0.213	0.802 (-1.623 – 3.228)	0.510	-48.286 (-152.199 – 55.627)	0.355
Radiotherapy	11.563 (-32.391 – 55.518)	0.600	-0.883 (-4.062 – 2.295)	0.579	50.568 (-85.623 – 186.758)	0.459
Adjuvant Chemotherapy	13.513 (-15.335 – 42.361)	0.351	-0.474 (-2.561 – 1.612)	0.650	-2.195 (-91.578 – 87.188)	0.961
PICO dressing	-38.828 (-66.328 - -11.328)	0.007**	-0.221 (-2.209 – 1.768)	0.825	-108.358 (-193.565 - -23.151)	0.014*
Mastectomy volume	0.111 (0.002 – 0.220)	0.045*	-0.001 (-0.008 – 0.007)	0.896	0.473 (0.136 – 0.810)	0.007*

[a), b), c)] Linear regression with coefficient for continuous variables

* $p < 0.05$, ** $p < 0.01$

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