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On the conservatism of multiple comparisons procedures among mean vectors

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Abstract: In this paper, conservative simultaneous confidence intervals for multiple comparisons among mean vectors in multivariate normal distributions are considered. Some properties of the multivarite Tukey-Kramer procedure for pairwise comparisons and a conservative procedure for comparisons with a control are presented, and the extent of conservativeness for the procedure for comparisons with a control is discussed.

Key Words and Phrases: comparisons with a control, conservativeness, coverage probability, pairwise multiple comparison, simultaneous confidence interval

1 Introduction

Consider the simultaneous confidence intervals for multiple comparisons among mean vectors from the multivariate normal populations. We discuss the extent of conservativeness for the multivariate Tukey-Kramer(T-K) pairwise comparisons procedure and for the conservative procedure on comparisons with a control by Seo(1995). Let $\boldsymbol{\mu}_i$ be the mean vector from ith population. Let $\boldsymbol{M} = [\boldsymbol{\mu}_1, \ldots, \boldsymbol{\mu}_k]$ be the unknown $p \times k$ matrix and $\widehat{\boldsymbol{M}} = [\widehat{\boldsymbol{\mu}}_1, \ldots, \widehat{\boldsymbol{\mu}}_k]$ be the estimator of $\boldsymbol{M}$ such that $\mathrm{vec}(\boldsymbol{X})$ is distributed as $N_{kp}(0, \boldsymbol{V} \otimes \boldsymbol{\Sigma})$, where $\boldsymbol{X} = \widehat{\boldsymbol{M}} - \boldsymbol{M}$, $\boldsymbol{V}$ is a known $k \times k$ positive definite matrix and $\boldsymbol{\Sigma}$ is an unknown $p \times p$ positive definite matrix, and $\mathrm{vec}(\cdot)$ denotes the column vector formed by stacking the columns of the matrix under each other. Also, let $\boldsymbol{S}$ be an unbiased estimator of $\boldsymbol{\Sigma}$ such that $\nu \boldsymbol{S}$ is independent of $\widehat{\boldsymbol{M}}$ and is distributed as a Wishart distribution $W_p(\boldsymbol{\Sigma}, \nu)$. Then the simultaneous confidence intervals for multiple comparisons among mean vectors are given by

$$a'Mb \in \left[\ a'\widehat{M}b \pm t(b'Vb)^{1/2}(a'Sa)^{1/2}\right], \quad \forall a \in \mathbb{R}^p,\ \forall b \in \mathbb{B}, \tag{1}$$

where $\mathbb{R}^p$ is the set of any nonzero real p-dimensional vectors and $\mathbb{B}$ is a subset that consists of r vectors in the k-dimensional space. We note that the value $t(>0)$ is the upper α percentile of the $T^2_{\max}$-type statistic,

$$T^2_{\max} = \max_{b \in \mathbb{B}} \left\{ \frac{(Xb)'S^{-1}Xb}{b'Vb} \right\}, \tag{2}$$

which the coverage probability for (1) is $1-\alpha$.

In many experimental situations, pairwise comparisons and comparisons with a control are standard for multiple comparisons. In the case of pairwise comparisons, we note that

$$\mathbb{B} = \mathbb{C} \equiv \{c \in \mathbb{R}^k : c = e_i - e_j,\ 1 \le i < j \le k\},$$

where e_i is the ith unit vector of the k-dimensional space. We can also express (1) as

$$a'(\mu_i - \mu_j) \in \left[\ a'(\widehat{\mu}_i - \widehat{\mu}_j) \pm t_{\max \cdot p}\ (d_{ij}a'Sa)^{1/2}\right], \forall a \in \mathbb{R}^p,\ 1 \le i < j \le k,$$

where $t^2_{\max \cdot p}$ is the upper α percentile of $T^2_{\max \cdot p}$ statistic,

$$T^2_{\max \cdot p} = \max_{i<j}\{(x_i - x_j)'(d_{ij}S)^{-1}(x_i - x_j)\},$$

and $d_{ij} = v_{ii} - 2v_{ij} + v_{jj}$.

In the case of pairwise comparisons and $V = I$, the $T^2_{\max}$ type statistic is reduced as the same as half of the multivariate studentized range statistic $R^2_{\max}$ which is an extension of the usual univariate studentized range (see, e.g., Seo and Siotani(1992)). Seo, Mano and Fujikoshi(1994) proposed the multivariate Tukey-Kramer procedure which is a simple procedure by replacing with the upper percentile of the multivariate studentized range statistic as an approximation to the one of $T^2_{\max}$ type statistic for any positive definite matrix V. This procedure is an extension of Tukey-Kramer procedure(Tukey 1953; Kramer 1956, 1957). The Tukey-Kramer procedure is an attractive and simple procedure for pairwise multiple comparisons. On the univariate case, it is shown in Dunnett(1980) that the generalized Tukey conjecture for pairwise comparisons by an extensive simulation study. Theoretical discussions related to this conjecture are referred to Hayter(1984, 1989), Brown(1984). It is known that this generalized conjecture is true for (i) $k = 3$(see, Brown(1984)) and (ii) d_{ij}'s satisfy $d_{ij} = a_i + a_j$ for some positive numbers a_i and a_j(see, Hayter(1989)), where $d_{ij} = v_{ii} - 2v_{ij} + v_{jj}$. Thus even for the univariate case, there has been no analytical proof of the generalized Tukey conjecture except the special cases. Further, Lin, Seppänen and Uusipaikka(1990) have discussed the generalized Tukey conjecture for pairwise comparisons among the components of the mean vector.

The multivariate generalized Tukey conjecture is known as the statement that the multivariate Tukey-Kramer procedure yields the conservative simultaneous confidence intervals for all pairwise comparisons among mean vectors. The multivariate version of the generalized Tukey conjecture has been affirmatively proved in the case of three correlated mean vectors by Seo, Mano and Fujikoshi(1994). Relating to this conjecture, Seo(1996) discussed how the approximate simultaneous confidence level by the multivariate Tukey-Kramer procedure is close to $1 - \alpha$. The related discussion for the univariate case is referred to Somerville(1993).

In the case of comparisons with a control, we have

$$\mathbb{B} = \mathbb{D} \equiv \{\boldsymbol{d} \in \mathbb{R}^k : \boldsymbol{d} = \boldsymbol{e}_i - \boldsymbol{e}_k,\ i = 1, \ldots, k-1\},$$

where k-th population is the control. Then we can write (1) as

$$\boldsymbol{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in [\, \boldsymbol{a}'(\widehat{\boldsymbol{\mu}}_i - \widehat{\boldsymbol{\mu}}_k) \pm t_{\max\cdot c}\ (d_{ik}\boldsymbol{a}'\boldsymbol{S}\boldsymbol{a})^{1/2}] \,, \forall \boldsymbol{a} \in \mathbb{R}^p,\ i = 1, \ldots, k-1.$$

where $t^2_{\max\cdot c}$ is the upper α percentile of $T^2_{\max\cdot c}$ statistic,

$$T^2_{\max\cdot c} = \max_{i=1,\ldots,k-1} \{(\boldsymbol{x}_i - \boldsymbol{x}_k)'(d_{ik}\boldsymbol{S})^{-1}(\boldsymbol{x}_i - \boldsymbol{x}_k)\}.$$

In this paper, we discuss the extent of conservativeness for the simultaneous confidence intervals for comparisons with a control in the case of three mean vectors. The organization of the paper is as follows. In Section 2, the extent of conservativeness for the multivariate Tukey-Kramer procedure is discussed. In Section 3, a conservative procedure for comparisons with a control by Seo(1995) is presented and its upper bound for the conservativeness is presented.

2 The multivariate Tukey-Kramer procedure

The simultaneous confidence intervals for all pairwise comparisons by the multivariate Tukey-Kramer procedure are given by

$$\boldsymbol{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[\ \boldsymbol{a}'(\widehat{\boldsymbol{\mu}}_i - \widehat{\boldsymbol{\mu}}_j) \pm t_p\sqrt{d_{ij}\boldsymbol{a}'\boldsymbol{S}\boldsymbol{a}}\right], \forall \boldsymbol{a} \in \mathbb{R}^p,\ 1 \le i < j \le k, \tag{3}$$

where ${t_p}^2$ is the upper α percentile of $T^2_{\max\cdot p}$ statistic with $\boldsymbol{V} = \boldsymbol{I}$, that is, $t_p^2 = q^2/2$ and $q^2 \equiv q^2_{p,k,\nu}(\alpha)$ is the upper α percentile of the p-variate studentized range statistic with parameters k and ν. By a reduction of relating to the coverage probability of (3), Seo, Mano and Fujikoshi(1994) proved that the coverage probability in the case $k = 3$ is equal or greater than $1 - \alpha$ for any positive definite matrix $\boldsymbol{V}$. Using the same reduction, Seo(1996) discussed the bound of conservative simultaneous confidence levels.

Consider the probability

$$Q(t, \boldsymbol{V}, \mathbb{B}) = \Pr\{\ (\boldsymbol{X}\boldsymbol{b})'(\nu \boldsymbol{S})^{-1}(\boldsymbol{X}\boldsymbol{b}) \le t(\boldsymbol{b}'\boldsymbol{V}\boldsymbol{b}),\ \forall \boldsymbol{b} \in \mathbb{B}\ \}, \tag{4}$$

where t is any fixed constant. Without loss of generality, we may assume $\boldsymbol{\Sigma} = \boldsymbol{I}_p$ when we consider the probability (4).

When $t^2 = {t_p^*}^2 = t_p^2/\nu$ and $\mathbb{B} = \mathbb{C}$, the coverage probability (4) is the same as the coverage probability of (3). The conservativeness of the simultaneous confidence intervals (3) means that $Q(t_p^*, \boldsymbol{V}, \mathbb{C}) \ge Q(t_p^*, \boldsymbol{I}, \mathbb{C}) = 1 - \alpha$. The inequality is known as the multivariate generalized Tukey conjecture. Then we have the following theorem for the case $k = 3$ by using same line of the proof of Theorem 3.2 in Seo, Mano and Fujikoshi(1994).

Theorem 1 *Let $Q(t_p^*, \boldsymbol{V}, \mathbb{C})$ be the coverage probability (3) for a positive definite matrix $\boldsymbol{V}$ and $t_p^* = q/\sqrt{2\nu}$. Then, for any $\boldsymbol{V}$, it holds that*

$$1-\alpha = Q(t_p^*, \boldsymbol{I}, \mathbb{C}) \le Q(t_p^*, \boldsymbol{V}, \mathbb{C}) < Q(t_p^*, \boldsymbol{V}_0, \mathbb{C}),$$

where $\boldsymbol{V}_0$ satisfies with one of $\sqrt{d_{ij}} = \sqrt{d_{il}} + \sqrt{d_{jl}}$, $i \neq j \neq l$.

This is the extended result of Seo(1996). As a conjecture, it may be expected that the inequality holds for general case $k \ge 4$.

For a special case that $\boldsymbol{V}$ is a diagonal matrix, we consider the statistic $T^2_{\max\cdot p}$ with the case $\boldsymbol{V} = \mathrm{diag}(n_1^{-1}, \dots, n_k^{-1})$. Then we have

$$T^2_{\max\cdot p} = \max_{i<j}\left[\frac{(\boldsymbol{x}_i - \boldsymbol{x}_j)'\boldsymbol{S}^{-1}(\boldsymbol{x}_i - \boldsymbol{x}_j)}{n_i^{-1} + n_j^{-1}}\right].$$

Without loss of generality, we can assume $n_i \le n_j$ and put $a_{ij}^2 = n_i/n_j$. Then we have

$$T^2_{\max\cdot p} = \max_{i<j}\left[\frac{(\boldsymbol{u}_i - a_{ij}\boldsymbol{u}_j)'\boldsymbol{S}^{-1}(\boldsymbol{u}_i - a_{ij}\boldsymbol{u}_j)}{1 + a_{ij}^2}\right],$$

where $\boldsymbol{u}_i = \sqrt{n_i}(\widehat{\boldsymbol{\mu}}_i - \boldsymbol{\mu}_i) \sim N_p(0, \boldsymbol{I})$ and $\nu\boldsymbol{S} \sim W_p(\boldsymbol{I}, \nu)$. Then, when $a_{ij} \to 0$, we have

$$T^2_{\max\cdot p} = \widetilde{T}^2_{\max} = \max_{i=1,\dots,k-1}\{\boldsymbol{u}_i'\boldsymbol{S}^{-1}\boldsymbol{u}_i\}.$$

Also, when $k = 3$, the distribution of $\widetilde{T}^2_{\max}$ statistic is the same as that of $T^2_{\max\cdot p}$ statistic with $\sqrt{d_{12}} = \sqrt{d_{13}} + \sqrt{d_{23}}$ or $\sqrt{d_{13}} = \sqrt{d_{12}} + \sqrt{d_{23}}$ or $\sqrt{d_{23}} = \sqrt{d_{12}} + \sqrt{d_{13}}$, that is, one of $\sqrt{d_{ij}} = \sqrt{d_{il}} + \sqrt{d_{jl}}$, $i \neq j \neq l$. From Theorem 1, it follows that $Q(t_p^*, \boldsymbol{V}, C) < \Pr\{\widetilde{T}^2_{\max} < t_p^{*2}\}$ for any diagonal matrix $\boldsymbol{V}$. Therefore, ewe have the following corollary.

Corollary 2 *Let $Q(t_p^*, \boldsymbol{V}, \mathbb{C})$ be the coverage probability (3) for a positive definite and diagonal matrix $\boldsymbol{V}$ and $t_p^* = q/\sqrt{2\nu}$. Then, for any $\boldsymbol{V}$, it holds that*

$$1-\alpha = Q(t_p^*, \boldsymbol{I}, \mathbb{C}) \le Q(t_p^*, \boldsymbol{V}, \mathbb{C}) < \Pr\{\widetilde{T}^2_{\max} < t_p^2\},$$

where

$$\widetilde{T}^2_{\max} = \max_{i=1,\dots,k-1}\{\boldsymbol{u}_i'\boldsymbol{S}^{-1}\boldsymbol{u}_i\},$$

and $\boldsymbol{u}_i$, $i = 1, \dots, k-1$ are independent identically distributed as $N_p(0, \boldsymbol{I})$ and $\nu\boldsymbol{S}$ is distributed as $W_p(\boldsymbol{I}, \nu)$.

3 A conservative procedure for comparisons with a control

In this section, a conservative procedure for comparisons with a control by Seo(1995) is discussed. The simultaneous confidence intervals for all comparisons with a control are given by

$$a'(\mu_i - \mu_k) \in \left[a'(\widehat{\mu}_i - \widehat{\mu}_k) \pm t_{\max\cdot c}\sqrt{d_{ik}a'Sa} \right], \forall a \in \mathbb{R}^p,\ i = 1, \dots, k-1, \quad (5)$$

where $t^2_{\max\cdot c} = t^2_c(\alpha; p, k, \nu, V)$ is the upper α percentile of $T^2_{\max\cdot c}$ statistic. Seo(1995) conjectured conservative simultaneous confidence intervals given by

$$a'(\mu_i - \mu_k) \in \left[a'(\widehat{\mu}_i - \widehat{\mu}_k) \pm t_c\sqrt{d_{ik}a'Sa} \right], \forall a \in \mathbb{R}^p,\ i = 1, \dots, k-1$$

with $t_c = t_c(\alpha; p, k, \nu, V_1)$ and V_1 satisfies with $d_{ij} = d_{ik} + d_{jk}$, $1 \le i < j \le k-1$. This conjecture has been affirmatively proved in the case of $k = 3$ by Seo(1995).

The coverage probability (4) with $t^2 = t_c^{*2} = t_c^2/\nu$ and $\mathbb{B} = \mathbb{D}$ is the same as the coverage probability of (5). Then we have the following theorem for the case $k = 3$.

Theorem 3 *Let $Q(t_c^*, V, \mathbb{D})$ be the coverage probability (5) for a positive definite matrix V and $t_c^{*2} = t_c^2(\alpha; p, k, \nu, V_1)/\nu$. Then, for any V, it holds that*

$$1 - \alpha = Q(t_c^*, V_1, \mathbb{D}) \le Q(t_c^*, V, \mathbb{D}) < Q(t_c^*, V_2, \mathbb{D}),$$

where V_1 satisfies with $d_{12} = d_{13} + d_{23}$ and V_2 satisfies with $\sqrt{d_{12}} = |\sqrt{d_{13}} - \sqrt{d_{23}}|$.

From Theorem 3, it is noted that the procedure with $t_c = t_c^*$ for multiple comparisons with a control yields the conservativeness for any positive definite matrix V when the case $k = 3$. For the case $k \ge 4$, we can conjecture that the following simultaneous confidence intervals are conservative.

$$a'Md \in \left[a'\widehat{M}d \pm t_c (d'Vd)^{\frac{1}{2}} (a'Sa)^{\frac{1}{2}} \right], \quad \forall a \in \mathbb{R}^p, \forall d \in \mathbb{D},$$

where $t_c = t_c(\alpha; p, k, \nu, V_1)$ and V_1 satisfies with the conditions $d_{ij} = d_{ik} + d_{jk}$, $1 \le i < j \le k-1$. That is, it may be expected that the procedure give the conservative and good approximate simultaneous confidence intervals. Further, we have the following corollary.

Corollary 4 *Let $Q(t_c^*, V, \mathbb{D})$ be the coverage probability (5) for a positive definite and diagonal matrix V. Then, for any V, it holds that*

$$1 - \alpha = \Pr\{\widetilde{T}^2_{\max} < t_c^2\} < Q(t_c^*, V, \mathbb{D}) < \Pr\{T_k^2 < t_c^2\},$$

where $t_c^{*2} = t_c^2/\nu$, t_c^2 is the upper α percentile of $\widetilde{T}^2_{\max}$ statistic defined in Corollary 2, and T_k^2 statistic is $np/(n-p+1)F_{p,n-p+1}$ statistic with p and $n-p+1$ degrees of freedoms.

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