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Evaluating the Performances of ROC Curve Estimation Methods for Different Distributions and Different Kernel Functions

Farklı Dağılımlar ve Farklı Çekirdek Fonksiyonları için ROC Eğrisi Tahmin Yöntemlerinin Performanslarının İncelenmesi

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ABSTRACT Objective: Receiver operating characteristic (ROC) curve is a statistical method used to examine the actual effectiveness of a diagnostic test or a biomarker in a comprehensive and reliable way. Several methods have been proposed to estimate ROC curve properly. The aim of the present study is to compare recent ROC curve estimation methods for different distribution and sample sizes. **Material and Methods:** Log-concave density and smooth log-concave density estimate based ROC curve estimation, kernel based ROC curve estimation with Gaussian, Epanechnikov, rectangular, triangular kernels, and binormal ROC estimation methods were compared for different simulation scenarios. **Results:** The ROC curve estimation methods based on kernel estimates gave their best performances when the biomarker values of non-diseased group are normal but the biomarker values of the diseased group are right-skewed, with a notable difference from other methods. Epanechnikov and rectangular kernel methods yielded better performance than other kernel methods in small sample sizes; but this difference disappeared as the sample size increased. The methods based on kernel or log-concave density estimate gave their worst results for the simulation scenario where the data were non-normal but symmetric. **Conclusion:** The performances of the other methods examined in the study exceeded the performance of the binormal method in highly skewed data in both groups and when the distribution of diseased and non-diseased populations were right-skewed and normal, respectively.

Keywords: Diagnostic test; receiver operating characteristic curve; kernel density estimation; log-concave density estimation

ÖZET Amaç: Alıcı işletim karakteristiği [receiver operating characteristic (ROC)] eğrisi, bir tanı testinin veya bir biyobelirtecin gerçek etkinliğini kapsamlı ve güvenilir bir şekilde incelemek için kullanılan istatistiksel bir yöntemdir. ROC eğrisini doğru bir şekilde tahmin etmek için çeşitli yöntemler önerilmiştir. Bu çalışmanın amacı, farklı dağılım ve örneklem büyüklükleri için güncel ROC eğrisi tahmin yöntemlerini karşılaştırmaktır. **Gereç ve Yöntemler:** Log-konkav yoğunluk ve düzgün log-konkav yoğunluk tahmini tabanlı ROC eğrisi tahmin yöntemi, Gaussian, Epanechnikov, dikdörtgen, üçgen kernel fonksiyonu kullanan kernel tabanlı ROC eğrisi tahmin yöntemleri ve binormal ROC eğrisi tahmin yöntemleri farklı simülasyon senaryoları kullanılarak karşılaştırılmıştır. **Bulgular:** Kernel tahmincilerine dayanan ROC eğrisi tahmin yöntemleri, sağlıklı grubun biyobelirteç değerlerinin normal dağılım, hasta grubun biyobelirteç değerlerinin sağa çarpık dağılım gösterdiği durumda, diğer yöntemlerden büyük farkla en iyi performansı göstermiştir. Epanechnikov vedikdörtgen kernel yöntemleri, diğer kernel yöntemlerinden küçük örneklemlerde daha iyi performans göstermekle birlikte aralarındaki fark, örneklem büyüklüğündeki artışla ortadan kalkmıştır. Kernel ve log-konkav yoğunluk tahminine dayalı yöntemler, verinin normal olmadığı fakat simetrik olduğu durumda en kötü sonucu vermişlerdir. **Sonuç:** Çalışmada incelenen yöntemlerin performansları, her iki grupta yüksek oranda çarpık veriler olması durumunda ve hasta ve sağlıklı popülasyonların dağılımları sırasıyla sağa çarpık dağılım ve normal dağılım olduğunda, binormal yöntemin performansını geçmiştir.

Anahtar kelimeler: Tanı testi; alıcı işlem karakteristik eğrisi; kernel yoğunluk tahmini; log-konkav yoğunluk tahmini

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In clinical decision making, it is important to distinguish patients and healthy individuals as accurately as possible, with diagnostic tests, which are evaluation methods based on laboratory techniques, clinical observations or original equipment measurements, used to identify a disease. Receiver operating characteristic (ROC) curve is a statistical method used to examine the actual effectiveness of a diagnostic test or a biomarker in a comprehensive and reliable way.[1-3] For the continuous diagnostic test results, sensitivity and specificity are being computed for all possible cut-off values which discriminate the subjects as diseased and non-diseased. The ROC curve shows the arrangement between sensitivity and the 1-specificity.[4]

Let $x_1, x_2, \dots, x_n$ and $y_1, y_2, \dots, y_m$ denote the test results of n subjects belonging to random sample from diseased population and m subjects belonging to random sample from non-diseased population; $F_X(.)$ and $G_Y(.)$ denote the cumulative distribution functions of the two independent random variables X and Y from the diseased and non-diseased populations respectively. For a given cut-off point c, the test result is positive if it is greater than c. So, the theoretical ROC curve can be defined as a plot of [1 - $G_Y(c)$, 1 - $F_X(c)$]. Let u be a possible false positive rate (FPR) corresponding to a cut-off point for positivity,

$$FPR = P(Y > c) = 1 - G_Y(c) = u\,. \tag{1}$$

Then one can write,

$$G_Y(c) = 1 - u \tag{2}$$

and

$$c = {G_Y}^{-1}(1 - u) \tag{3}$$

Hence, sensitivity [true positive rate (TPR)] can be given as $TPR = P(X > c) = 1 - F_X(c)$. So, ROC curve can be given as in equation-4.

$$ROC(u) = 1 - F_X[G_Y^{-1}(1 - u]. \tag{4}$$

Also assume that all observations in the diseased and non-diseased samples are mutually independent and empirical distribution function related to diseased sample and quantile function related to non-diseased sample are defines as $\hat{F}_X(.)$ and ${\hat{G}_Y}^{-1}(.)$, respectively. When there is no knowledge about the underlying distributions of both samples and so $F_X(.)$ and $G_Y(.)$ have completely unknown structures functions, plugging the empirical counterparts into the equation-1, yields a non-parametric ROC curve estimation method, namely empirical ROC curve estimation.[5,6] Although it is robust and represents data accurately, especially for small sample sizes it has a problem of variability and as it is a step function there can be different *Food Programs Reporting Systems* for a TPR value, and vice versa. Besides, the estimated ROC curve being in a jagged form, since the true ROC curve is a smooth curve, it underestimates the true ROC curve.[7,8] Another approach is the parametric ROC curve estimation which assumes that the $F_X(.)$ and $G_Y(.)$ have a known structure and which computes the ROC curve based on the estimates of these distribution functions. The most prevalent choice for these functions is the cumulative distribution function of a standard normal distribution, which gives the binormal ROC curve as given in equation-5, where $\alpha = (\mu_X - \mu_Y)/\sigma_X$ and $\beta = \sigma_Y/\sigma_X$.[4] In equation-5, α and β are estimated by using sample estimates of population means and standard deviations of diseased and healthy populations.

$$ROC(u) = \Phi\left[\alpha + \beta\Phi^{-1}(u)\right] \tag{5}$$

But parametric ROC curves have some distributional assumptions. Several methods have been explored to estimate a ROC curve more precisely. These include using kernel estimates of $F_X(.)$ and $G_Y(.)$ in equation-4.[9-11] Let $f(.)$ and $g(.)$ be the probability density functions of random variables X and Y from the dis-

eased and non-diseased populations, and $\tilde{f}(.)$ and $\tilde{g}(.)$ are their kernel estimates, respectively. One can write,

$$\tilde{f}(x) = \frac{1}{nh_d}\sum_{i=1}^{n} k_d\left(\frac{x-x_i}{h_d}\right) \quad (6)$$

and

$$\tilde{g}(y) = \frac{1}{mh_n}\sum_{i=1}^{n} k_n\left(\frac{y-y_i}{h_n}\right) \quad (7)$$

where h_d and h_n are the bandwidths, k_d and k_n are the kernel functions for diseased and non-diseased populations. Zou et al. suggested estimating the points on the ROC curve by using the integral of kernel estimates.[9] By taking the integrals of $\tilde{f}(x)$ and $\tilde{g}(y)$ to the right of threshold one can get $\tilde{F}(x)$ and $\tilde{G}(y)$. Plugging these estimates in equation-4, new ROC curve estimation has been obtained.

Rufibach has proposed to use log-concave density estimates and also kernel smoothed version of the log-concave probability density function, instead of kernel function, which can be used for asymmetric and unimodal densities.[12] The density function $f(.)$ is called log-concave if it is in the form $f(x) = \exp\ \varphi(x)$ for some concave function $\varphi: \mathrm{R} \to [-\infty, \infty]$. For a sample of independent and identically distributed random variables $X_1, \ldots, X_n$ from $f(x)$, the density estimate was calculated by maximizing the log-likelihood function

$$\ell(\varphi) = n^{-1}\sum_{i=1}^{n} \varphi(X_i) \quad (8)$$

over all functions φ that are concave and produce a probability density.[13] Rufibach defined smooth ROC curve estimator by computing log-concave distribution function estimates of $F_X(.)$ and $G_Y(.)$ both for diseased and non-diseased samples, and then plugging these estimates in equation-4.[12]

In the present paper, we aimed to compare the performances of different ROC curve estimation methods; including estimators derived from kernel estimators including different kernel functions, estimators derived from log-concave density estimates and fully parametric binormal method, for the diagnostic test results coming from different distributions with different sample sizes. Also to investigate the impact of different kernel functions on the performance of a ROC curve estimation, we compared four different kernel functions.

MATERIAL AND METHODS

We performed a simulation study to compare the performances of different methods for different scenarios given in Table 1. Scenario-1 serves as a benchmark for comparing other estimators to the binormal model, which both the biomarker values of both non-diseased and diseased populations are symmetric and normal. It has been customary to assume that the biomarker values for the non-diseased population may be normal but diseased population to be non-normal and right-skewed in diagnostic studies. Scenario-2 is used to simulate data for this situation, where the biomarker values of non-diseased group is normal, but the diseased group is non-normal and skewed. Scenario-3 is used to evaluate the performance of ROC curve estimators, in situation both distributions are right-skewed, where data generated from gamma distribution. Scenario-4 is used in situation both distributions are highly right-skewed where data generated from exponential distribution. Scenario-5 is used to for symmetric but non-normal distributions, where data generated from lognormal distribution. Scenarios have been selected similar with the related studies in the literature, to allow the results to be analogous.[12,14,15]

TABLE 1: Scenarios used in the simulation study.

Scenario	Diseased	Non-diseased	n-m
1	$N(1,1)$	$N(0,1)$	20-20 50-50 100-100 200-200
2	$Gamma(2,1)$	$N(2,1)$	
3	$Gamma(4,1.5)$	$Gamma(2,1)$	
4	$Exponential(\lambda = 1/4.6)$	$Exponential(\lambda = 1/2.5)$	
5	$Lognormal(2,1)$	$Lognormal(0,1)$	

We compared seven methods which are fully parametric binormal method, log-concave and smooth log-concave methods proposed by Rufibach, and four ROC curve estimation method based on kernel estimation proposed by Zou.[9,12] In fully parametric binormal model, we estimated α and β in equation-5 directly from the mean and variance of the underlying distributions. For kernel based ROC curve estimators, we used four different kernel functions; namely Gaussian, Epanechnikov, rectangular and triangular kernel. The method of Sheather and Jones was used for bandwidth selection.[16] As all the kernels are symmetrical, first of all we normalized the data with quantile normalization as suggested by Robin et al.[17] To ensure standardization, we performed normalization for all methods.

We computed $\widehat{ROC}(u)$ values for u_i grid points, $i = 1, 2, \dots, n_{grid}$.. We compared the results using average square error (ASE), a generally used index for evaluating performance of an ROC curve estimator $\widehat{ROC}(u)$, for the true ROC curve $ROC\ (u)$. ASE has been defined as in equation-9.[12,14,15]

$$ASE = \frac{\sum_{i=1}^{n_{grid}} (\widehat{ROC}(u_i) - ROC(u_i))^2}{n_{grid}} \quad (9)$$

In the simulation study, we took n_{grid}=500 and the number of repetition was taken as r=1000. R 4.0.4 software used for the simulations. pROC package was used for the ROC curve estimation methods except the binormal method.

RESULTS

The mean, standard deviation and standard error of the ASE values for each simulation scenarios described in Table 1 are given. The results are presented in Table 2 for Scenario-1, Table 3 for Scenario-2, Table 4 for Scenario-3, Table 5 for Scenario-4 and Table 6 for Scenario-5.

TABLE 2: Average square error values for the ROC curve estimation of different methods for the biomarker values from the diseased population are $X \sim N(1,1)$ and from the non-diseased population are $Y \sim N(0,1)$.

Method		**n=20**	**n=50**	**n=100**	**n=200**
Full parametric binormal	Mean	0.00850	0.00345	0.00168	0.00081
	SD	0.01024	0.00440	0.00209	0.00108
	SEM	0.00032	0.00014	0.00007	0.00003
Based on kernel estimate-Gaussian kernel	Mean	0.08194	0.08003	0.07851	0.07867
	SD	0.02628	0.02020	0.01846	0.01654
	SEM	0.00083	0.00064	0.00058	0.00052
Based on kernel estimate-Epanechnikov kernel	Mean	0.08189	0.08002	0.07850	0.07867
	SD	0.02619	0.02016	0.01845	0.01653
	SEM	0.00083	0.00064	0.00058	0.00052
Based on kernel estimate-Rectangular kernel	Mean	0.08188	0.08001	0.07850	0.07867
	SD	0.02616	0.02015	0.01844	0.01652
	SEM	0.00083	0.00064	0.00058	0.00052
Based on kernel estimate-Triangular kernel	Mean	0.08191	0.08002	0.07850	0.07867
	SD	0.02622	0.02017	0.01845	0.01653
	SEM	0.00083	0.00064	0.00058	0.00052
Based on log-concave density estimate	Mean	0.08772	0.08360	0.08229	0.08024
	SD	0.04896	0.03068	0.02178	0.01438
	SEM	0.00155	0.00097	0.00069	0.00045
Based on smooth log-concave density estimate	Mean	0.08596	0.08284	0.08188	0.08003
	SD	0.04743	0.03013	0.02154	0.01429
	SEM	0.00150	0.00095	0.00068	0.00045

SD: Standard deviation; SEM: standard error of mean.

TABLE 3: Average square error values for the ROC curve estimation of different methods for the biomarker values from the diseased population are $X \sim Gamma(2,1)$ and from the non-diseased population are and $Y \sim N(2,1)$.

Method		**n=20**	**n=50**	**n=100**	**n=200**
Full parametric binormal	Mean	0.01420	0.00807	0.00642	0.00542
	SD	0.01469	0.00739	0.00521	0.00349
	SEM	0.00046	0.00023	0.00016	0.00011
Based on kernel estimate-Gaussian kernel	Mean	0.00989	0.00939	0.00884	0.00844
	SD	0.00694	0.00555	0.00475	0.00434
	SEM	0.00022	0.00018	0.00015	0.00014
Based on kernel estimate-Epanechnikov kernel	Mean	0.00984	0.00937	0.00883	0.00844
	SD	0.00692	0.00554	0.00474	0.00434
	SEM	0.00022	0.00018	0.00015	0.00014
Based on kernel estimate-Rectangular kernel	Mean	0.00983	0.00937	0.00883	0.00844
	SD	0.00692	0.00554	0.00474	0.00434
	SEM	0.00022	0.00018	0.00015	0.00014
Based on kernel estimate-Triangular kernel	Mean	0.00985	0.00938	0.00883	0.00844
	SD	0.00693	0.00554	0.00474	0.00434
	SEM	0.00022	0.00018	0.00015	0.00014
Based on log-concave density estimate	Mean	0.01858	0.01153	0.00969	0.00824
	SD	0.01731	0.00950	0.00661	0.00427
	SEM	0.00055	0.00030	0.00021	0.00014
Based on smooth log-concave density estimate	Mean	0.01708	0.01095	0.00938	0.00808
	SD	0.01641	0.00923	0.00649	0.00422
	SEM	0.00052	0.00029	0.00021	0.00013

SD: Standard deviation; SEM: Standard error of mean.

TABLE 4: Average square error values for the ROC curve estimation of different methods for the biomarker values from the diseased population are $X \sim Gamma(4,1.5)$ and from the non-diseased population are and $Y \sim Gamma(2,1)$.

Method		**n=20**	**n=50**	**n=100**	**n=200**
Full parametric binormal	Mean	0.01555	0.00738	0.00484	0.00328
	SD	0.01736	0.00725	0.00425	0.00230
	SEM	0.00055	0.00023	0.00013	0.00007
Based on kernel estimate-Gaussian kernel	Mean	0.03495	0.03337	0.03337	0.03223
	SD	0.01662	0.01214	0.01214	0.01113
	SEM	0.00053	0.00038	0.00038	0.00035
Based on kernel estimate-Epanechnikov kernel	Mean	0.03490	0.03276	0.03335	0.03222
	SD	0.01661	0.01349	0.01214	0.01113
	SEM	0.00053	0.00043	0.00038	0.00035
Based on kernel estimate-Rectangular kernel	Mean	0.03489	0.03276	0.03335	0.03222
	SD	0.01657	0.01347	0.01213	0.01112
	SEM	0.00052	0.00043	0.00038	0.00035
Based on kernel estimate-Triangular kernel	Mean	0.03492	0.03277	0.03336	0.03222
	SD	0.01659	0.01349	0.01213	0.01113
	SEM	0.00052	0.00043	0.00038	0.00035
Based on log-concave density estimate	Mean	0.04599	0.03760	0.03474	0.03382
	SD	0.03557	0.02227	0.01577	0.01110
	SEM	0.00112	0.00070	0.00050	0.00035
Based on smooth log-concave density estimate	Mean	0.04528	0.03746	0.03471	0.03382
	SD	0.03430	0.02185	0.01559	0.01102
	SEM	0.00108	0.00069	0.00049	0.00035

SD: Standard deviation; SEM: Standard error of mean.

TABLE 5: Average square error values for the ROC curve estimation of different methods for the biomarker values from the diseased population are $X \sim Exponential(\lambda = 1/4.6)$ and from the non-diseased population are and $Y \sim Exponential(\lambda = 1/2.5)$.

Method		**n=20**	**n=50**	**n=100**	**n=200**
Full parametric binormal	Mean	0.05467	0.04227	0.03660	0.03252
	SD	0.02878	0.01794	0.01151	0.00807
	SEM	0.00091	0.00057	0.00036	0.00026
Based on kernel estimate-Gaussian kernel	Mean	0.02747	0.02688	0.02614	0.02594
	SD	0.01408	0.01190	0.00987	0.00926
	SEM	0.00045	0.00038	0.00031	0.00029
Based on kernel estimate-Epanechnikov kernel	Mean	0.02743	0.02686	0.02613	0.02594
	SD	0.01404	0.01188	0.00986	0.00926
	SEM	0.00044	0.00038	0.00031	0.00029
Based on kernel estimate-Rectangular kernel	Mean	0.02742	0.02686	0.02613	0.02594
	SD	0.01402	0.01188	0.00986	0.00926
	SEM	0.00044	0.00038	0.00031	0.00029
Based on kernel estimate-Triangular kernel	Mean	0.02744	0.02687	0.02613	0.02594
	SD	0.01405	0.01189	0.00987	0.00926
	SEM	0.00044	0.00038	0.00031	0.00029
Based on log-concave density estimate	Mean	0.03612	0.03073	0.02901	0.02788
	SD	0.03014	0.01965	0.01340	0.00908
	SEM	0.00095	0.00062	0.00042	0.00029
Based on smooth log-concave density estimate	Mean	0.03467	0.03013	0.02870	0.02771
	SD	0.02910	0.01930	0.01327	0.00903
	SEM	0.00092	0.00061	0.00042	0.00029

SD: Standard deviation; SEM: Standard error of mean.

TABLE 6: Average square error values for the ROC curve estimation of different methods for the biomarker values from the diseased population are $X \sim Lognormal(2,1)$ and from the non-diseased population are and $Y \sim Lognormal(0,1)$.

Method		n=20	n=50	n=100	n=200
Full parametric binormal	Mean	0.00964	0.00452	0.00255	0.00150
	SD	0.01119	0.00526	0.00281	0.00005
	SEM	0.00035	0.00017	0.00009	0.00092
Based on kernel estimate-Gaussian kernel	Mean	0.10381	0.10501	0.10467	0.10493
	SD	0.02735	0.02341	0.02037	0.01858
	SEM	0.00086	0.00074	0.00064	0.00059
Based on kernel estimate-Epanechnikov kernel	Mean	0.10377	0.10500	0.10467	0.10493
	SD	0.02727	0.02337	0.02035	0.01857
	SEM	0.00086	0.00074	0.00064	0.00059
Based on kernel estimate-Rectangular kernel	Mean	0.10377	0.10499	0.10467	0.10493
	SD	0.02723	0.02335	0.02034	0.01857
	SEM	0.00086	0.00074	0.00064	0.00059
Based on kernel estimate-Triangular kernel	Mean	0.10378	0.10500	0.10467	0.10493
	SD	0.02730	0.02338	0.02035	0.01858
	SEM	0.00086	0.00074	0.00064	0.00059
Based on log-concave density estimate	Mean	0.11623	0.11092	0.10792	0.10728
	SD	0.05288	0.03404	0.02335	0.01730
	SEM	0.00167	0.00108	0.00074	0.00055
Based on smooth log-concave density estimate	Mean	0.11395	0.10992	0.107915	0.10699
	SD	0.05109	0.03342	0.02334655	0.01720
	SEM	0.00162	0.00106	0.000738283	0.00054

SD: Standard deviation; SEM: Standard error of mean.

DISCUSSION

Statistical modeling of ROC curves is a vast topic and offers several future research lines. In the present study, we compared the performances of recently proposed several ROC curve estimation methods, using different techniques to smooth the ROC curve, in different simulation scenarios.

As expected, the ROC estimators from fully parametric binormal model yielded the best performance when the data follow normal distribution in both groups. It is observed that the kernel based estimates were better than the log-concave density based estimates when the data follow normal distribution in both groups. In kernel based ROC curve estimation methods, although the difference was not notable, Epanechnikov and rectangular kernel gave the best performances for Scenario-1. The ROC curve estimation method based on the smooth log-concave density estimate was better than the log-concave density estimate when the data follow normal distribution in both groups.

When the distribution of the biomarker values of non-diseased group is normal, but the diseased groups is non-normal and skewed (Scenario-2), the performance of the full parametric binormal ROC curve estimation decreased dramatically. However, the ASE values were still smaller that the that of the ROC curve estimation methods based on the log-concave density estimate and smooth log-concave density estimate. Again, smooth version of the log-concave density estimate yielded better results than the log-concave density estimate. On the other hand, methods based on kernel estimates gave best results compared to other methods. The performances of kernel based methods for this scenario were similar to the results of full parametric binormal method in case of Scenario-1. Especially in small samples, Epanechnikov and rectangular kernel methods yielded better performance than other kernel methods; but it has been seen that this difference disappeared as the sample size increased.

When the distributions of both diseased and non-diseased population are moderately right-skewed, (both generated from gamma distribution, i.e. Scenario-3), it was not surprising that the full parametric binormal model gave slightly better results than the other methods, since the skewness of the data was not very high level. On the other hand, for small sample size, full parametric binormal model performed worse than it did in Scenario-2, where diseased population is right-skewed and the non-diseased population follow normal distribution. But it gave better performance than that it did in Scenario-2 for moderate and large sample sizes. The ROC estimation methods based on kernel estimation gave slightly worse performances than the full parametric binormal method for Scenario-3. Estimates based on log-concave and smooth log-concave density estimates yielded the worse results. Kernel and log-concave density estimate based ROC estimation methods could not outperform the binormal method although the biomarker distributions were right-skewed in diseased and non-diseased populations.

For the situation where both distributions are highly right-skewed and data generated from exponential distribution (Scenario-4), the ROC estimation methods based on kernel and log-concave density estimates, finally outperformed the performance of fully parametric binormal ROC method. The difference between the binormal ROC method and other methods decreased as the sample size increased. Kernel methods also yielded better performances that that of log-concave density based methods. Especially in small and moderate samples, rectangular and Epanechnikov kernel methods yielded better performance than the other kernel methods; but this difference disappeared in big sample sizes. Again, smooth log-concave density estimate gave better results that the log-concave density estimate based method.

For the Scenario-5 where data generated from lognormal distribution, the full parametric binormal ROC estimation method gave the best results according to the other methods. This can be the result of that the distribution of both groups were symmetric. The results for the full parametric binormal model in this situation was similar to its performance in Scenario-1. It was surprising that the ROC estimation methods based on kernel or log-concave density gave their worst results among all the scenarios. It is seen that the performances of the methods except the binormal model did not affected much from the increase in sample size.

It was not surprising that all the methods gave better results as the sample size increased for all scenarios. However, the impact of the sample size was more pronounced for the full parametric binormal method and the methods based on log-concave density and smooth log-concave density estimates. The impact of the sample size was smaller when the data of both were highly right-skewed.

CONCLUSION

Full parametric binormal ROC curve estimation method gave its best performance in two situations, where the biomarker values of both diseased and non-diseased populations follow normal distribution and where the biomarker values of two populations follow lognormal distribution, differing greatly from the other methods. The results of the present study showed that the binormal method performed well in symmetric but non-normal distribution, too. The ROC curve estimation methods based on kernel estimates gave their best performances when the biomarker values of non-diseased group are normal but the biomarker values of the

diseased group are right-skewed, with a notable difference from other methods. The performances of the other methods examined in the study did not exceed the performance of the binormal method in moderately skewed data, but surpassed it in highly skewed data.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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